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ADAPTING AND EVALUATING A HOSPITAL2HOME CASE CONFERENCE SERVICE FOR PATIENTS WITH SEVERE PROGRESSIVE IDIOPATHIC FIBROTIC INTERSTITIAL LUNG DISEASE

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**ADAPTING AND EVALUATING A HOSPITAL2HOME
CASE CONFERENCE SERVICE FOR PATIENTS WITH
SEVERE PROGRESSIVE IDIOPATHIC FIBROTIC
INTERSTITIAL LUNG DISEASE**

Dr Sabrina Bajwah MBChB, MRCP, MSc, MA

This thesis is submitted incorporating publications in
fulfilment of the requirements for the degree of Doctor of
Philosophy

Abstract

Patients with Progressive Idiopathic Fibrotic Interstitial Lung Diseases (PIF-ILD) have a median survival of 3 years. Research into the palliative care needs of these patients is limited. The Hospital2Home (H2H) case conference (CC) is a new multi-professional, patient centred intervention at the end-of-life. Individualised care plans provide a comprehensive Palliative Care assessment with follow up. Research into use of H2H in the UK or the non-malignant setting has not been carried out.

This thesis describes a study which aimed to develop and evaluate H2H in PIF-ILD. The study followed the Medical Research Council's (MRC) guidance on developing and evaluating complex interventions, focussing on the Development and Feasibility/Piloting stages and using a sequential mixed methods study design. The Development stage included a systematic review which showed a paucity of interventions to improve symptoms and quality of life (QoL). Qualitative in-depth interviews of 18 patients, informal caregivers and HPs showed that patients had uncontrolled symptoms which profoundly impacted on every part of patients' and informal caregivers' lives. There was good understanding of the terminal nature of PIF-ILD but a poor understanding of prognosis. All participants were positive about H2H.

The adapted H2H model was trialled in a fast-track Randomised Controlled Trial (RCT) forming the Feasibility/Piloting stage. 122 patients were screened of which 53 were randomised. The primary outcome was mean change in Palliative Care Outcome Score (POS) at 4 weeks- Fast-Track -5.7 (7.5) vs Waiting List -0.4 (8.0) $p=0.02$. There were also improvements in patient QoL, anxiety and depression scores and informal caregiver anxiety and depression scores. The intervention and study design were largely both feasible and acceptable.

Findings from this PhD suggest that H2H may improve palliative care needs, QoL and anxiety and depression in PIF-ILD. Further research is needed to evaluate these results in a larger Evaluation trial.

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This PhD is dedicated to my late father- Bashir Ahmed Bajwah- to whom I owe everything.

Publications, posters and oral presentations

Publications in peer reviewed journals

The following publications have been incorporated into chapters in the thesis:

Bajwah S, Ross JR, Peacock JL, Higginson IJ, Wells AU, Patel A, Koffman J, Riley J. Interventions to improve symptoms and QoL of patients with fibrotic ILD: a systematic review of the literature. *Thorax* 2013;**68**:9 867-879 **CHAPTER 1**

Bajwah S, Higginson IJ, Ross JR, Wells AU, Birring SS, Patel A, Riley J. Specialist palliative care is more than drugs: a retrospective study of ILD patients. *Lung* 2012;190(2):215-20 **CHAPTER 1**

Bajwah S, Koffman J, Higginson IJ, Ross JR, Wells AU, Birring SS, Riley J. "I wish I knew more...." - the end-of-life planning and information needs for end-stage fibrotic interstitial lung disease: views of patients, informal caregivers and HP. *BMJ Supportive & Palliative Care* 2013;3:84-90 **CHAPTER 4**

Bajwah S, Koffman J, Higginson IJ, Ross JR, Wells AU, Birring SS, Riley J. The palliative care needs for fibrotic interstitial lung disease: A qualitative study of patients, informal caregivers and HP. *Palliative Medicine* 2013;27(9):869-876 **CHAPTER 4**

Bajwah S, Ross JR, Wells AU, Mohammed K, Oyeboode C, Birring SS, Koffman J, Higginson IJ, Riley J. Palliative Care for Patients with Advanced Fibrotic Lung Disease: a randomised controlled phase II and feasibility trial of a case conference intervention. *Thorax* doi:10.1136/thoraxjnl-2014-206583 **CHAPTER 5**

Posters, oral presentations and published abstracts

Bajwah S, Koffman J, Higginson IJ, Ross JR, Wells AU, Biring SS, Riley J.

The needs and experiences of progressive idiopathic fibrotic interstitial lung disease patients, informal caregivers and HP: a qualitative study-*Poster and presentation at British Thoracic Winter Meeting Dec 2011*

Bajwah S, Koffman J, Higginson IJ, Ross JR, Wells AU, Biring SS, Riley J.

ILD: from bench to bedside and back again: P87 The needs and experiences of progressive idiopathic fibrotic interstitial lung disease patients, informal caregivers and HP: a qualitative study. *Thorax* 2011;66:Suppl 4 A103 doi:10.1136/thoraxjnl-2011-201054c.87-*published abstract*.

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Bajwah S, Higginson IJ, Ross JR, Wells AU, Biring SS, Riley J.

Symptom burden, psychological and spiritual concerns of patients with Progressive Idiopathic Fibrotic Interstitial Lung Disease.-*Poster presented at European Association Palliative Care Congress, Lisbon- May 2011*

Bajwah S, Higginson IJ, Ross JR, Wells AU, Biring SS, Riley J. Symptom Burden, Psychological and Spiritual Concerns of Patients with Progressive Idiopathic Fibrotic Interstitial Lung Disease. EAPC Scientific Congress, Lisbon, Portugal. *European Journal of Palliative Care* 2011; P316- *published abstract*.

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Bajwah S, Higginson IJ, Ross JR, Wells AU, Biring SS, Patel A, Riley J.

Specialist Palliative Care is more than drugs-a retrospective study of ILD patients

Oral presentation at European Respiratory Society Meeting, Amsterdam-September 2011

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Bajwah S, Higginson IJ, Ross JR, Wells AU, Koffman J, Biring SS, Riley J.

Developing and evaluating a Hospital2Home palliative care service for patients with advanced Progressive Idiopathic Fibrotic Interstitial Lung Disease: Phase 0-II-*Poster presented at European Association Palliative Care Congress - June 2012*

Bajwah S, Higginson IJ, Wells A.U., Koffman J, Ross JR, Birring SS, Riley J. 2012. Developing and Evaluating a Hospital2Home Palliative Care Service for Patients with Advanced Progressive Idiopathic Fibrotic Interstitial Lung Disease: Phase 0-II. *Palliative Medicine*. 26 (4): 545 (Abstract: P208)- *published abstract*.

Bajwah S, Ross JR, Peacock JL, Higginson IJ, Wells AU, Patel A, Koffman J, Riley J. Interventions to improve symptoms and QoL of patients with fibrotic ILD: a systematic review of the literature.- *Poster and presentation British Thoracic Winter Meeting Dec 2012*

Bajwah S, Ross JR, Peacock JL, Higginson IJ, Wells AU, Patel A, Koffman J, Riley J. Asthma outcomes: P131 What is the Evidence For Pharmacological and Non-Pharmacological Interventions in Improving Dyspnoea, Other Symptoms and QoL in Progressive Idiopathic Fibrotic Interstitial Lung Disease?- A Systematic Review of the Literature. *Thorax* 2012;67:Suppl 2 A118-A119 doi:10.1136/thoraxjnl-2012-202678.414- *published abstract*.

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Introduction

Interstitial lung disease (ILD) results in progressive inability to maintain normal blood oxygen levels due to impaired transfer of gas across the alveolar-capillary membrane.(1) ILD includes a variety of conditions all of which share the common characteristics of lung scarring and progressive loss of the normal gas transfer ability.(2) Where the cause is unknown and disease is progressive, this is will be referred to as Progressive Idiopathic Fibrotic Interstitial Lung Disease (PIF-ILD).

There are over 5,000 new cases of PIF-ILD each year in England and Wales, with a similar number of deaths.(3) The most common disease in this group is idiopathic pulmonary fibrosis (IPF) with an overall incidence rate during 2000-2008 in UK primary care of 7.44 per 100,000 person years.(3)

Patients with PIF-ILD have irreversible disease with no effective curative options. Patients experience a progressive loss of functional ability and, ultimately die from acute respiratory failure. However, survival varies widely;(4) Some patients die within one year of diagnosis, whereas others live longer than six years.(5, 6) Median survival from diagnosis in the UK is approximately 3 years.(7, 8) IPF is predominately a disease of later life, with two-thirds of patients being over 60 years old at presentation(9) with survival being poorest in those diagnosed later in life. This demographic profile is important as the incidence is set to double by 2030 as populations age.(10)

The UK End of Life Care Strategy has highlighted the importance of developing effective palliative care interventions for non-malignant diseases.(11) In addition, the British Thoracic Society guidelines for the management of patients with ILD include recommendations on the management of IPF patients which include “liaison with palliative care specialists”.(12)

Despite awareness that patients with IPF have poor QoL, no primary research has been conducted to guide palliative care delivery. Before palliative care can be delivered to this disease group it is essential that the needs of these patients and informal caregivers must be fully described and understood. It is important to then build on this work to develop and evaluate appropriate palliative care interventions.

This study therefore aims to explore the palliative care needs of patients and informal caregivers with PIF-ILD, to then adapt a case conference (CC) model of care (Hospital2Home, H2H) for PIF-ILD patients and their informal caregivers and then evaluate it in terms of feasibility and acceptability whilst gathering preliminary data on possible effects on patients and informal caregivers. The Medical Research Council's (MRC) guidance on the development and evaluation of complex interventions (13) has been used as the methodological approach (supported by the MOREcare guidance(14)) and within this, a mixed methods design has been adopted.

Overview of thesis

As each phase of the study (the PhD as a whole) has influenced the next, I have presented the chapters with methods and results for each phase. An overview of the chapters is presented here:

Chapter 1 is the background chapter for the study and comprises the following components: i) I will firstly present details of the pathophysiology and epidemiology of PIF-ILD ii) I will then explain what palliative care is and its potential role in the care of those living with PIF-ILD iii) I will explain both the MRC guidance on developing and evaluating complex interventions and the subsequent MOREcare guidance on developing interventions for End of Life Research iv) I will describe the Hospital2Home model of care and discuss how it may be adapted for the PIF-ILD group. As part of the *identifying the evidence base* phase of the MRC guidance, the published paper of the systematic review examining the evidence base for current interventions to improve symptoms and quality of life (QoL) in PIF-ILD will be presented v) I will discuss the current evidence of the palliative care needs of patients and informal caregivers with PIF-ILD (forming part of the *identifying the evidence base* phase of the MRC guidance) vi) I will then present the published retrospective review of medical notes to gain some preliminary understanding of the palliative care needs of these patients which will form the background for the *identifying or developing theory* phase of the MRC guidance vii) I will present a theoretical model of how an adapted H2H intervention may work in this group.

Chapter 2 outlines the aims and objectives of this study.

Chapter 3 presents an overview of the methods for the study. This includes discussion of how the MRC guidance (supported by the MOREcare guidance) will be used in developing and evaluating the H2H intervention, the rationale and the use of mixed methods and finally how integration of the mixed methods will be used within the MRC guidance.

Chapter 4 i) presents the aims and methods of the qualitative work ii) presents the results of the qualitative work used to build on the evidence base for the palliative care needs of patients with PIF-ILD. This builds on the evidence base of the palliative care needs of these patients and informal caregivers presented in Chapter 1 forming part of the *identifying theory/developing* theory stage of the Development Phase of the MRC guidance iii) the results of the qualitative work forming the *modelling theory/processes* phase are presented iv) a summary of all the findings for the *modelling theory/processes* phase will be presented and integration of the results from the systematic review, retrospective review of case notes and qualitative work will follow to produce the adapted H2H model of care.

Chapter 5 will form the Feasibility and Piloting stage of the MRC guidance. I will initially present aims of the RCT and then the submitted paper followed by more detailed methods, results and discussion.

Chapter 6 will form the overall Summary and Discussion chapter for the study.

Chapter 1 Background

1.1 Introduction

In this chapter I will present details of the pathophysiology and epidemiology of PIF-ILD. Secondly, I will discuss what palliative care is and its potential role in the care of those living with PIF-ILD. Thirdly, I will describe the MRC guidance on developing and evaluating complex interventions and the subsequent MOREcare guidance on developing interventions for End of Life Research. Fourthly, I will describe the Hospital2Home case conference model of care (H2H) which is used in the cancer setting and how it may be adapted for the PIF-ILD group. I will then present research conducted identifying the evidence base for current interventions to improve symptoms and quality of life (QoL) in PIF-ILD and the limited research available on the supportive care and QoL needs of these patients. Fifthly, I will discuss the current evidence of the palliative care needs of patients and informal caregivers with PIF-ILD (forming part of the *identifying the evidence base* part of the MRC guidance). I will then present the published retrospective review of medical notes conducted as background work to gain some preliminary understanding of the palliative care needs of these patients which will form the background for the *identifying or developing theory* part of the MRC guidance. Finally, I will present a theoretical model of how the adapted H2H intervention may work in this patient and informal caregiver group.

1.2 Interstitial Lung Disease

ILD refers to a group of conditions affecting the interstitium of the lung, all of which share the common characteristics of lung scarring and progressive loss of the normal gas transfer ability.⁽²⁾ There are almost 300 distinct injurious or inflammatory causes of ILD that can result in diffuse lung scarring and many others arise for no obvious reason and are termed idiopathic.⁽¹⁵⁾ Typically, lung scarring serves as a valuable healing role following injury.⁽¹⁶⁾ However, the lung may become progressively scarred following more chronic and/or repeated injuries, resulting in abnormal function.⁽¹⁶⁾ If a significant proportion of the lung becomes scarred, respiratory failure can occur.⁽¹⁶⁾

The main ILD diseases that are fibrotic (resulting in scarring) and progressive in nature are Idiopathic Pulmonary Fibrosis (IPF) and Non-Specific Interstitial Pneumonia (NSIP). For the purposes of this study, these diseases will be collectively referred to as Progressive Idiopathic Fibrotic Interstitial Lung Disease (PIF-ILD). Hamman and Rich are generally considered to have been the first to describe IPF as a new clinical and pathological entity.(17) Classification of these diseases within the wider ILD scheme is shown in Figure 1-1 Page 19 .

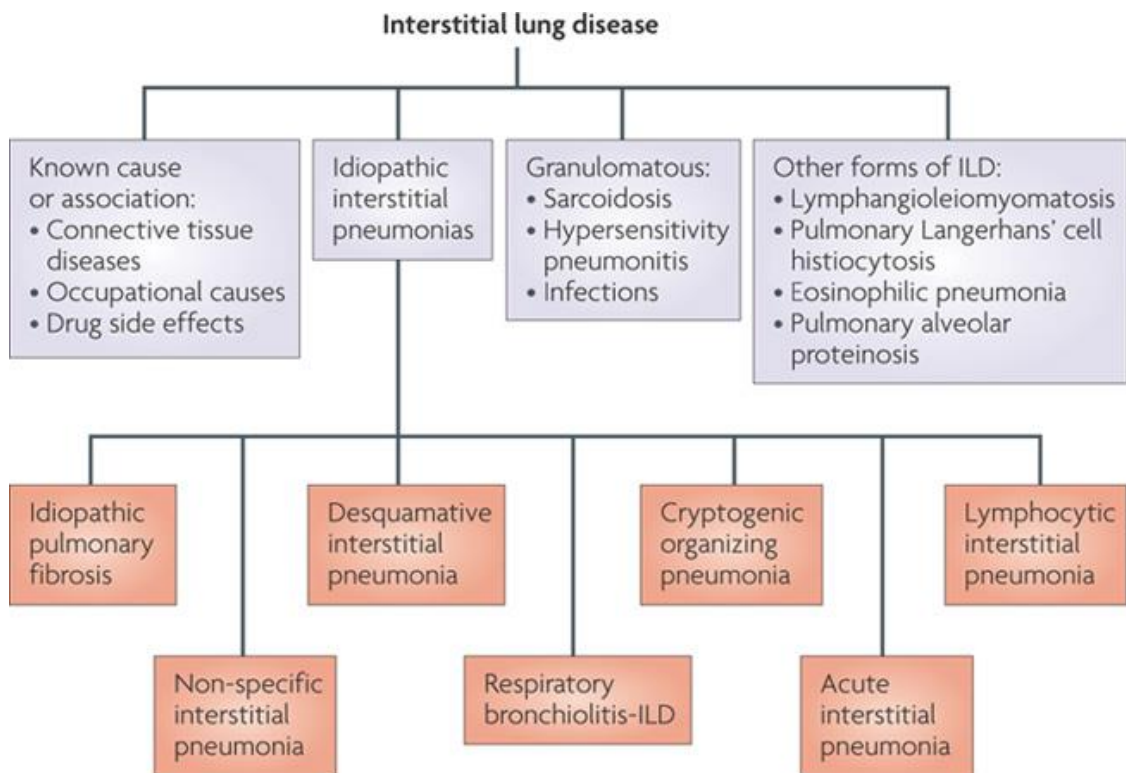


Figure 1-1 Classification of interstitial lung diseases including IPF and NSIP (16)

There are at least 5,000 new cases of PIF-ILD each year in England and Wales, with a similar number of deaths.(3) This means that in the UK, more people will die each year from PIF-ILD than from ovarian cancer, lymphoma, leukaemia, mesothelioma or renal cancer.(3) The most common disease in this group is IPF with an overall incidence rate during 2000-2008 in UK primary care of 7.44 per 100,000 person years.(3) Death registration in the UK analysed between 1968 and 2008 showed a six fold increase across the study period from 0.92 per 100,000 in the 1968-1972 calendar periods to 5.10 per 100,000 in the 2006-2008 calendar

period.(3) This was supported by primary care data from the same study. In both data sets, the size of the increase was 5% per year and this was not explained by ageing of the population.(3)

At present there are approximately 15,000 people in the UK with a PIF-ILD diagnosis.(3) Patients with IPF have irreversible disease with no effective curative treatment options. Patients experience a progressive loss of functional ability and ultimately, die from acute respiratory failure. However, survival varies widely.(4) Some patients die within one year of diagnosis, whereas others live longer than six years.(5, 6) Median survival from diagnosis in the UK is approximately 3 years.(7, 8) IPF is predominately a disease of later life, with two-thirds of patients being over 60 years old at presentation(9) with survival being poorest in those diagnosed later in life (Figure1-2 Page 20). This demographic profile is important as the incidence is set to double by 2030 as populations age.(10)

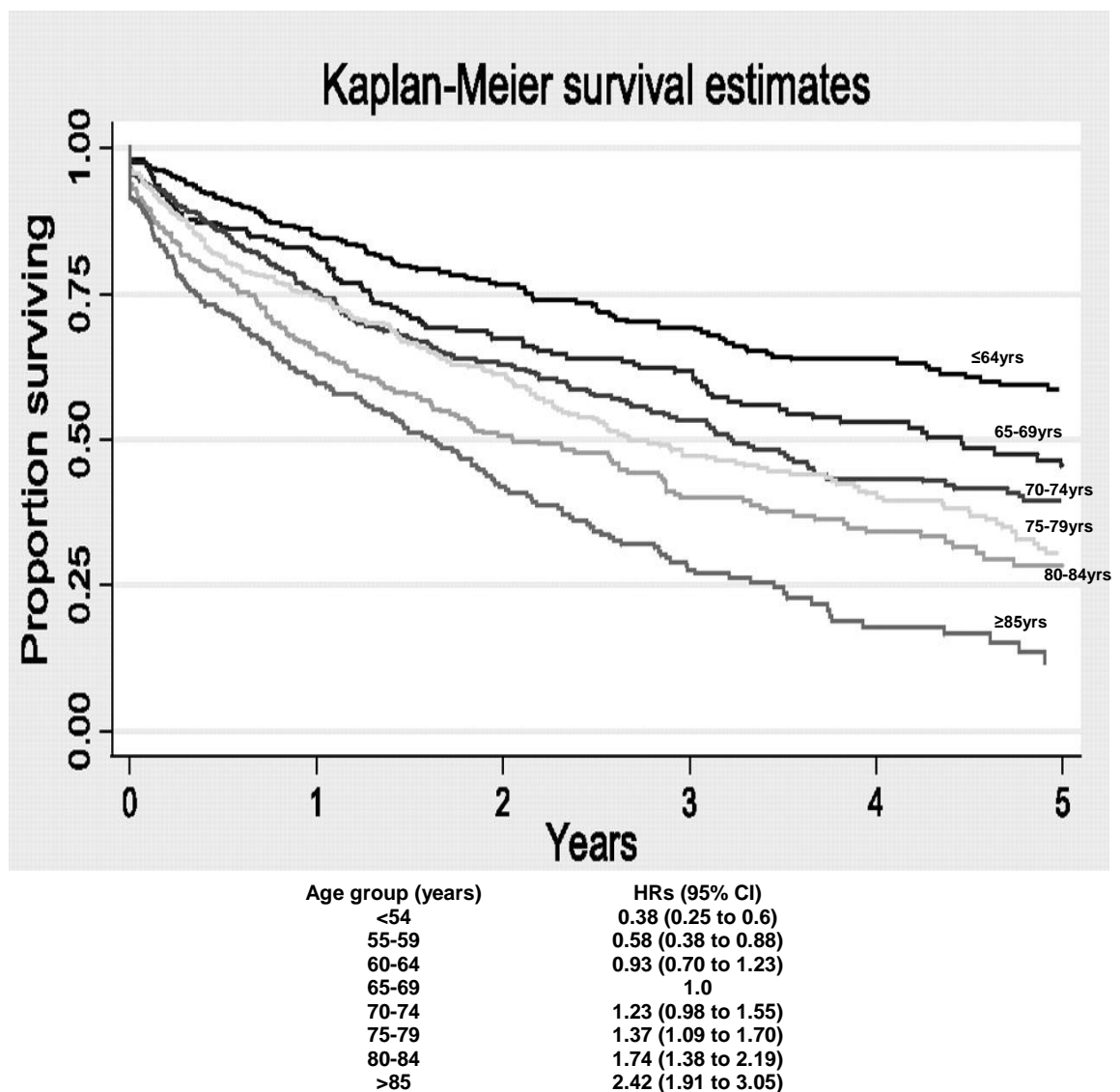


Figure 1-2 Kaplan Meir survival estimates stratified by age at time of diagnosis for IPF using the THIN (The Health Improvement Network) data set of n=2074 as found by Navaratnam et al.(3)

The clinical manifestation of fibrotic NSIP is similar to IPF.(18) It is important to differentiate NSIP from IPF in the early stages when the disease is potentially responsive to therapy.(18) However, when the disease is advanced and irreversible, this becomes less important as the disease is no longer responsive to treatment. Fibrotic NSIP follows a similar survival pattern to IPF. Figure 1-3 Page 21 shows comparison of survival of fibrotic NSIP and IPF. As the clinical manifestations of advanced fibrotic NSIP and IPF and survival patterns are similar, the two diseases will be considered together and be referred to as PIF-ILD.

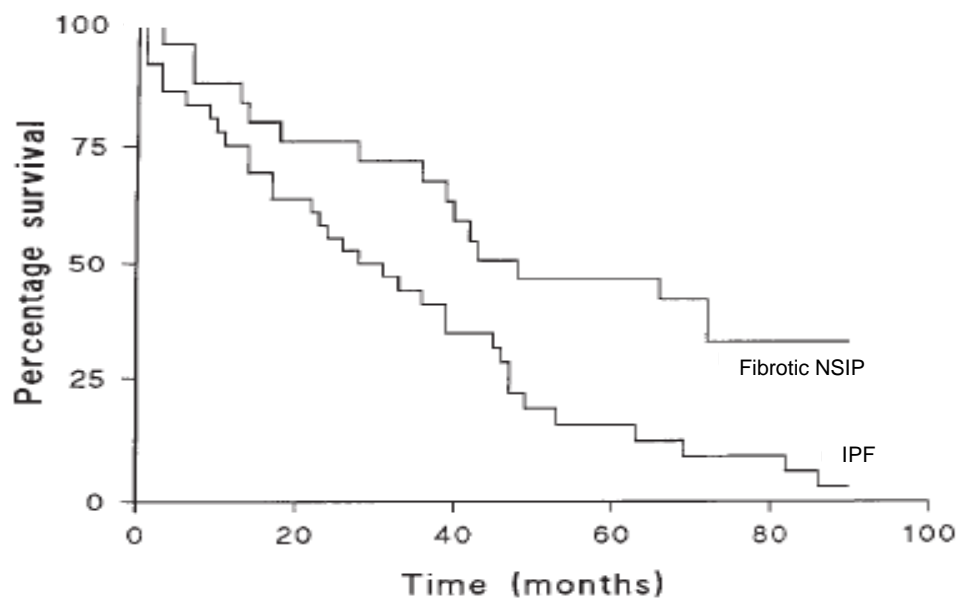


Figure 1-3 Survival of IPF compared to fibrotic and cellular NSIP in biopsy diagnosed ILD patients (n=78) as found by Nicholson et al. (19)

1.3 Palliative Care and PIF-ILD

Palliative Care is defined by the World Health Organisation as being:

“.....an approach that improves the QoL of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual....using a support system to help patients live as actively as possible until death, a support system to help the family cope during the patients illness and in their own bereavement and using a team approach to address the needs of patients and their families, including bereavement counselling, if indicated”.(20)

Survival is as poor for PIF-ILD as it is for many cancers(3) who traditionally receive palliative care. The UK End of Life Care strategy has highlighted the importance of developing effective palliative care interventions for non-malignant diseases.(11) In addition, the British Thoracic

Society guidelines for the management of patients with ILD include recommendations on the management of IPF patients. These state:

“Best supportive care should be considered a specific and important treatment strategy in all patients with IPF. It is a proactive approach to symptomatic treatment and may include oxygen therapy, pulmonary rehabilitation, opiates, antireflux therapy, withdrawal of steroids and other immunosuppressants, early recognition of terminal decline and liaison with palliative care specialists.”(12)

Importantly, this is supported by the 2013 NICE clinical guidelines on the diagnosis and management of IPF(21) which recommend considering referral to palliative care where appropriate. Historically, ILD patients have been largely managed by general respiratory services. However, there is now a drive for these patients to be managed in specialist centres which are adhering to NICE guidance. Consideration of the role of palliative care in the management of these patients and informal caregivers is therefore needed.

Palliative care has predominantly focussed on management of cancer at the end of life. However, non-malignant lung disease has a high mortality and symptom burden and encompasses various pathologies including chronic obstructive pulmonary disease (COPD), cystic fibrosis (CF), pulmonary hypertension, neuromuscular disorders and infections.(22) The physical and psychosocial needs of patients with these chronic lung diseases at EOL are comparable to those with lung cancer.(23) Despite survival and prognosis rates as poor as many cancers and an awareness that these patients have specific palliative care needs (24-27), primary research to quantify the needs of PIF-ILD patients or guide delivery is limited.

It is important to understand the needs of other non-malignant diseases. However, PIF-ILD is an individual group of diseases which has some similarity to diseases such as COPD in that they share the commonality of both being non-malignant progressive respiratory diseases that experience breathlessness. However, are the palliative care needs in PIF-ILD different? The palliative care needs in PIF-ILD are likely to relate in part to symptoms but also to the lack of recognition to the palliative care needs of PIF-ILD by HPs. Does this may make PIF-ILD unique in its disease journey for both patients and informal caregivers and influence the experiences of those living with the disease? Before palliative care can be delivered to PIF-ILD patients and

informal caregivers, it is essential that the needs and experiences of these patients and informal caregivers must be further described and understood.

1.4 Use of the Medical Research Council Guidance supported by the MORECare Statement

The MRC framework for developing and evaluating complex interventions was first developed in 2000.(28) This framework was then updated in 2008 and is now referred to as the MRC guidance.(13) Complex interventions have traditionally been defined as “interventions with several interacting components” where the active ingredient(s) may be difficult to identify.(13) This guidance aimed to help researchers to adapt appropriate methods whilst recognising that the extra problems of developing and evaluating complex interventions related to the difficulty of standardising the design and delivery of the interventions,(29, 30) their sensitivity to features of the local context (31, 32) and the complexity of the relationship between interventions and outcome.(33) The MRC guidance addresses how there are several dimensions of complexity. Palliative care interventions are likely to be a complex interventions. For example, a palliative care intervention usually involves a prescribing component and a number of interactions between multi-disciplinary team members, the patient and informal caregiver. In addition, delivery of the intervention itself occurs in variable settings (hospital, hospice or home) and is dependent of local service provision. Similarly, if you were to have a palliative care intervention in ILD, it is likely to be a complex intervention. The development and evaluation of a palliative care intervention poses challenges in identifying the individual and interdependent effects of components and choosing reliable outcome measures.

The MRC guidance counsels how the researcher deals with the complexity is reliant on the aims of the evaluation.(13) The two are inextricably linked. However, once effectiveness has been established, the intervention may be modified in an iterative manner as required. Fundamental questions are how does the intervention work, what are the vital constituents and how do the constituents fit together to exert their effect? (13, 34)

The MRC guidance advises:

‘Best practice is to develop interventions systematically, using the best available evidence and appropriate theory, then to test them using a carefully phased approach, starting with a series

of pilot studies targeted at each key uncertainties in the design, and moving on to an exploratory and then a definitive evaluation.’(13)

The MRC framework consists of four stages: **Feasibility and Piloting**, **Development**, **Evaluation** and **Implementation**. The previous linear framework has been replaced with a model that allows movement between each stage in the guidance (see Figure 1-4 Page 24).(13)

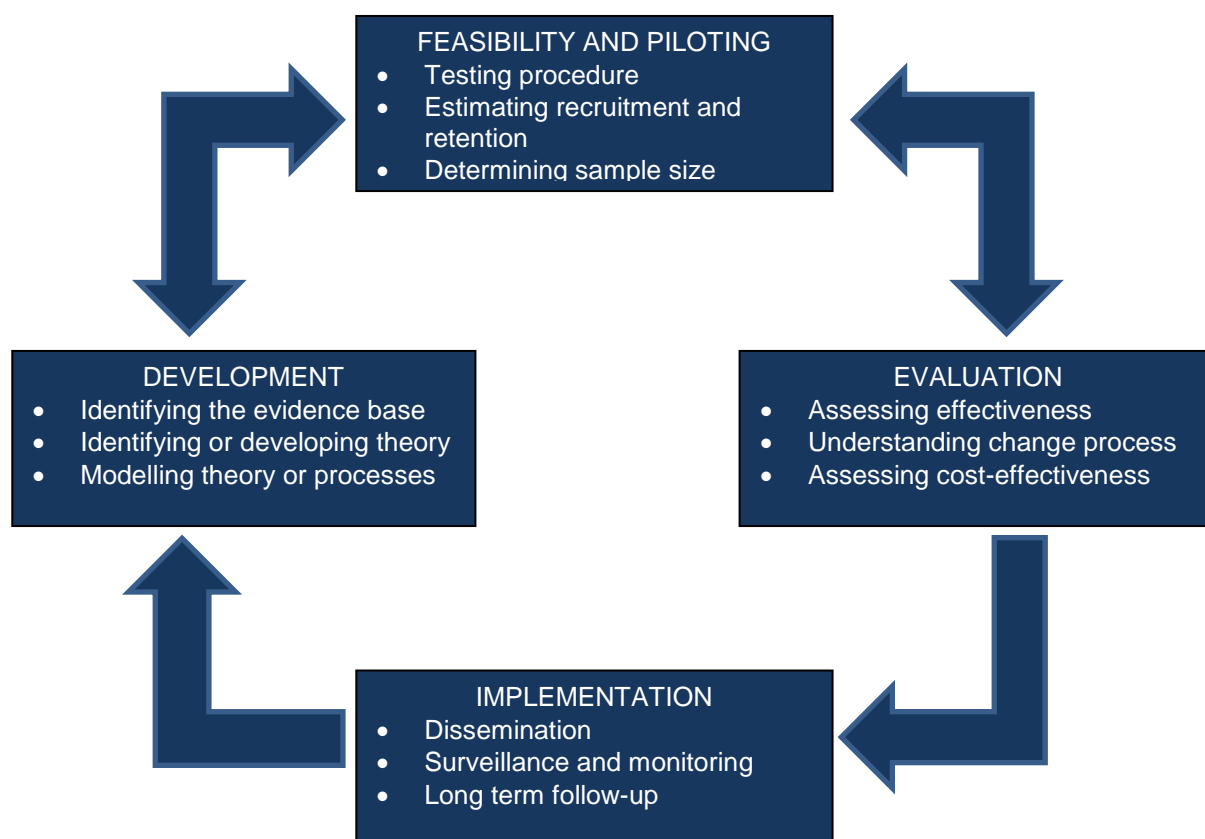


Figure 1-4 Key elements of the development and evaluation process of the MRC guidance (13)

The MRC guidance (13) stresses the importance of the **Development** phase and advises where possible to conduct a systematic review to *identify the existing evidence base*. In addition, it advises the importance of developing a theoretical understanding of “what changes are expected, and how change is to be achieved”. This should be done through identifying and appreciating existing evidence. However, if this evidence is not available, conducting new research on stakeholders ought to be conducted. Through amalgamation of existing and new evidence, a deeper understanding of the theoretical model of how the complex intervention may work is then achieved in the *identifying/developing theory* phase.(13)

In the *modelling theory or processes* phase, understandings and perceptions from the theory stage are used to develop the intervention and gain a comprehension into how the intervention

may affect the relationship between intervention and outcome.(13) In addition, the researcher must identify who needs to know about the outcome of the evaluation and what kind of information they will require in order to implement the changes that may be indicated and what kind of obstacles/difficulties may be encountered.(13)

The **Feasibility and Piloting** stage includes amongst other things, *testing procedure* (including testing methods for their acceptability and feasibility), *estimating the likely rates of recruitment and retention* of participants and the *determination of appropriate sample sizes* for the evaluation study(ies).(13) The **Feasibility and Piloting** stage should aim to address all the uncertainties identified in the **Development** stage. The MRC guidance stresses the importance of this stage. This stage may be repeated multiple times (interspersed with repeated visits to the **Development** stage as needed) before moving on to the formal evaluation of the complex intervention in the **Evaluation** stage. (13)

The Methods of Researching End of Life Care (MORECare) project provides guidance on the development and evaluation of complex end of life care (EoLC) research.(14) This project took the MRC guidance for developing and evaluating complex interventions as its basis and then conducted a phased study of systematic literature reviews, transparent expert consultations and stakeholder workshops to identify challenges and best practice in EoLC research. A guidance statement was then produced on the best methods to research EoLC research. Please see Table 1-1 Page 26. This guidance will be used alongside the MRC guidance.

Table 1-1 MORECare Statement- Checklist of components that require consideration when designing EoLC interventions (14)

Recommendations	
Introduction	<p>1. Present theoretical framework for the intervention and levels of need established</p> <p>2. Present objectives appropriate to the level of intervention development</p>
Study design	<p>3. Indicate and justify stage in MRC guidance for development and evaluation of complex interventions, for example, feasibility, preliminary evaluation, efficacy/cost effectiveness and wider effectiveness</p> <p>4. Feasibility stages should test both feasibility of the intervention and of methods of evaluation, including outcome measurement</p> <p>5. Justify methods, considering appropriate use of existing data sets and secondary analysis as these may produce rapid information</p> <p>6. Justify methods of empirical studies considering mixed methods, observational studies and randomised trials</p>
Study team	<p>7. Ensure involvement from: (i) consumers, patients and caregivers; (ii) relevant clinicians; (iii) relevant methodologists to develop study questions, questionnaires and procedures; and (iv) researchers familiar with the challenges in EoLC studies</p> <p>8. Ideally, involvement should be well established and continuing, beyond a specific study, with joint meetings or rotations between clinical and research staff</p>
Ethics	<p>9. Note in ethics committee application MORECare recommendations that it is ethically desirable for patients and families in EoLC to be offered involvement in research and MORECare evidence of patient willingness to be approached</p> <p>10. Work within legal frameworks on mental capacity, consent and so on, to ensure that those who may benefit from interventions are offered an opportunity to participate if they wish</p> <p>11. Collaborate with patients and caregivers in the design of the study, vocabulary used in explaining the study, consent procedures and any ethical aspects</p> <p>12. Attend the ethics committee meeting with a caregiver or patient, as a means to help the committee better understand the patient perspective</p> <p>13. Ensure proportionality in patient and caregiver information sheets, appropriate to the study design and level of risk, as excessive information in itself can be tiring/distressing for very ill individuals</p>
Participants	<p>14. Adjust eligibility criteria to recruit those patients who may benefit most from intervention, ensuring equipoise</p>
Procedures	<p>15. Minimise burden for existing clinical staff for participation in the study</p> <p>16. Clearly distinguish between service received and research activity interviews in study arms when multiple interviews with patients are undertaken in trials, for example, using a graphical system</p>
Outcome measures	<p>17. Choose outcome measures that meet the following criteria:</p> <ul style="list-style-type: none"> • established validity and reliability in relevant population • responsive to change over time • capture clinically important data • easy to administer and interpret (for example, short and with low level of complexity) • applicable across care settings to capture change in outcomes by location (for example, patients' home, hospital, hospice) • able to be integrated into clinical care • minimise problems of response shift (see below) <p>18. Consider including patients' experience of care, as this is central to many interventions</p> <p>19. Select time points of outcome measurement to balance the value of early recording, to reduce attrition, but to allow enough time for the intervention to have had an effect</p> <p>20. Consider the potential effect of response shift (that is, a change in a person's internal conceptualisation or calibration of the aspects measured). Questionnaires that include anchor points or descriptions of each response category may be less problematic in this regard</p>
Missing data & attrition	<p>21. Estimate in advance levels of, and reasons for, attrition and missing data, integrating these into sample size estimates and planned collection of data from proxies</p> <p>22. Monitor during the study and report all levels of, and reasons for, attrition and other missing data</p> <p>23. Assume missing quantitative data NOT to be at random unless proven otherwise</p> <p>24. Test results from different methods of imputation – noting that 'using only complete cases' is a form of imputation</p> <p>25. Use the MORECARE classification of attrition to describe causes of attrition: that is,</p> <ul style="list-style-type: none"> • ADD – attrition due to death; • ADI - attrition due to illness; • AAR - attrition at random. <p>26. Consider reasons for missing data which are not due to attrition, for example missed questionnaire, or missed data item in questionnaire. Consider these in analysis and the potential imputations</p>
Mixed methods studies	<p>27. Mixed methods can be appropriate in all phases of development and evaluation</p> <p>28. Ensure appropriate multi-disciplinary skills mix or training of team</p> <p>29. Define the theoretical paradigm and method of integrating results and safeguards to ensure rigour at the outset</p> <p>30. Plan investigation to avoid undue burden of qualitative and quantitative questionnaires – perhaps dividing data collection or selecting questions and/or sampling appropriately</p> <p>31. Take into account any potential therapeutic effect of qualitative interviews where participants can express their feelings, if these are similar to components of the intervention</p> <p>32. Ensure that those collecting data are appropriately trained in qualitative data collection</p>
Implementation	<p>33. Consider implementation implications, including workforce and training needs, in all phases of the study</p>

1.5 The Hospital2Home case conference: an example of a complex intervention

In the UK, a case conference (CC) model of care (Hospital2Home, H2H) has been used in cancer patients at the Royal Marsden Hospital for the last 3 years. The H2H CC is a multi-professional, patient centred meeting for people nearing the end-of-life. The patient, the informal caregiver, H2H clinical nurse specialist (CNS), GP, district nurse, social worker and community palliative care CNS attend a CC in the patient's home. Current and anticipated care needs are discussed, and an action plan is agreed which allocates a responsible health care professional for each item. Individualised care plans provide a quality comprehensive palliative care assessment. This is then communicated with local services aiming to result in streamlining of transfer of data and codifying responsibility for the patient, informal caregiver and HPs. The aim is for follow up care to be provided by the community HPs. The patient and informal caregiver may contact the H2H CNS if there are difficulties in implementation of the care plan or breakdown in care and the H2H CNS will aim to resolve any issues by liaising with the relevant community HPs.

The H2H CC model of care is unique as it has the advantages of a CC (multi-professional, holistic, coordinated and integrated services across providers improving co-ordination of care and communication) and a care plan (care individualised to each patient and informal caregiver), but in addition there is a designated HP (the H2H CNS) who will follow up the CC with the patient/informal caregiver (at a 2 week, 1 month and 2 month interval) and is available as a point of contact to intervene for the patient and informal caregiver if the care plan were to breakdown.

The H2H model represents a complex intervention for the following reasons:

1. The H2H CC in its present form involves targeting multiple HPs as well as the patient and informal caregiver across both hospital and community settings.

2. There are several outcomes which may be changed by the intervention (including symptom control, QoL and health service use). This is also complex as these outcomes inter-relate.
3. There is flexibility in the intervention which may be tailored to individual patients, across settings and to this disease group.

An audit of 308 cancer patients at the Royal Marsden Hospital in which H2H was used, has shown that 47% patients died at home and 36% in hospice.(35) This equated to 83% congruence between actual and preferred place of death. However, the sample is likely to have been biased to those who wanted to die at home. Formal assessment in a trial of how H2H may affect place of death has not been conducted. A longitudinal trial looking at other outcomes such as symptom control, QoL and resource utilisation is currently underway at the Royal Marsden Hospital. The CC model of care or H2H has not been used in non-malignant terminal disease. It is possible that H2H may be effective as a complex palliative care intervention for the PIF-ILD group.

In developing and evaluating H2H for the PIF-ILD group, the MRC guidance for developing and evaluating complex interventions will be used.(13) The **Development** and **Feasibility and Piloting** stages have been conducted for this thesis. In addition, the MOREcare guidance (14) will also be followed to ensure best practice in developing this EoLC intervention.

1.6 Current interventions to improve symptom control and QoL needs

The MRC guidance advises that the first step in developing and evaluating a complex intervention is to first assess the existing evidence base through a systematic review.(13)

I have therefore conducted a systematic review identifying and appraising interventions to improve symptoms and QoL in PIF-ILD. This research forms part of the **Development** stage of the MRC guidance in *identifying the evidence base* for palliative interventions in this group. The published paper will be presented followed by a summary of the findings.

- 1.6.1 **Bajwah S, Ross JR, Peacock JL, Higginson IJ, Wells AU, Patel A, Koffman J, Riley J. Interventions to improve symptoms and QoL of patients with fibrotic ILD: a systematic review of the literature. THORAX 2013;68:9 867-87**

Interventions to improve symptoms and quality of life of patients with fibrotic interstitial lung disease: a systematic review of the literature

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► Additional data are published online only. To view the files please visit the journal online (<http://dx.doi.org/10.1136/thoraxjnl-2012-202040>).

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ABSTRACT

Background Patients with fibrotic interstitial lung disease have symptom control and quality of life (QoL) needs. This review aims to evaluate the evidence for the use of interventions in improving dyspnoea, other symptoms and QoL.

Methods Eleven databases, relevant websites and key journals were hand-searched. Studies were assessed and data extracted independently by two researchers using standardised proformas. Meta-analyses were performed where possible with 95% CI.

Results 34 papers with 19 interventions in 3635 patients were included. Meta-analyses showed no significant effect of interferon- γ -1b or sildenafil on 6-minute walking distance (6MWD) or dyspnoea. Pulmonary rehabilitation and pirfenidone had a positive effect on 6MWD (mean difference (95% CI) 27.4 (4.1 to 50.7) and 24.0 (4.3 to 43.7), respectively), and pulmonary rehabilitation had a mixed effect on dyspnoea. Both pulmonary rehabilitation and sildenafil showed a trend towards significance in improving QoL. There was weak evidence for the improvement of 6MWD using oxygen; dyspnoea using prednisolone, diamorphine, D-penicillamine and colchicine; cough using interferon α and thalidomide; anxiety using diamorphine; fatigue using pulmonary rehabilitation; and QoL using thalidomide and doxycycline. A wide range of outcome scales was used and there were no studies with economic evaluation.

Conclusions There is strong evidence for the use of pulmonary rehabilitation and pirfenidone to improve 6MWD and moderate evidence for the use of sildenafil and pulmonary rehabilitation to improve QoL. Future recommendations for research would include careful consideration of the dichotomy of radical and palliative treatments when deciding on how symptom and QoL outcome measures are used and data presented.

INTRODUCTION

Patients with interstitial lung disease have a wide range of diagnoses and prognoses. Many patients can live many years with their diagnosis and some are responsive to treatments. However, a subset of patients with progressive idiopathic fibrotic interstitial lung diseases (PIF-ILD), such as idiopathic pulmonary fibrosis (IPF), have a short disease trajectory and a similar prognosis to patients with lung cancer.¹

Only a small number of patients are suitable for lung transplantation and no other treatments have been shown to influence mortality. Evidenced-based palliation is seldom applied, despite the high symptom burden² and poor quality of life (QoL).³

What is the key question?

- What is the overall outcome of trials assessing the use of pharmacological and non-pharmacological methods to improve symptom control and QoL in patients with progressive idiopathic fibrotic interstitial lung diseases?

What is the key point?

- There is strong evidence for the use of pulmonary rehabilitation and some evidence for sildenafil and pirfenidone. There is weak evidence for a number of other interventions which warrants further investigation.

Why read on?

- All patients with progressive idiopathic fibrotic interstitial lung diseases should receive best supportive care to improve symptom control and QoL and, where possible, this should be evidence-based.

In this systematic review of PIF-ILD, we evaluate (1) the evidence for the use of interventions to improve symptoms and QoL; (2) the evidence for the use of symptom scales for dyspnoea and other symptoms; and (3) the cost-effectiveness of interventions to improve symptoms and QoL. In addition, we aim to make a crucial distinction between radical (potentially disease-modifying) and palliative (non-disease-modifying) treatments, and consider this in appraising the evidence as interpretation of secondary outcome measures should differ between these contexts.

METHODS

Search strategy

We performed comprehensive searches of 11 electronic databases including MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL) from 1966 to December 2010 using a combination of MESH headings and keywords (for full search strategy see online appendix 1). In addition, three key respiratory journals (*Thorax*,

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American Journal of Respiratory and Critical Care Medicine and *Chest*) were hand-searched for the last 3 years, with reference lists of all included papers. The search was updated to September 2011. Study authors were contacted to obtain full reports where abstracts only were available or further information was required (authors contacted twice in 1 month period). No language restrictions were imposed and translation was performed where needed.

Selection

Study populations

Published data for patients diagnosed with IPE, non-specific interstitial pneumonia (NSIP), cryptogenic fibrosing alveolitis (CEA) and idiopathic interstitial pneumonia (IIP) were evaluated. All stages of disease were included. Studies including subjects with other forms of ILD were acceptable if outcomes for PIF-ILD were reported separately. Where necessary, authors were contacted and, if no separate data was obtainable, the study was excluded but listed as potentially relevant.

Types of interventions

Any single or combined interventions for the treatment of PIF-ILD were reviewed including pharmacological and non-pharmacological treatments, with the exception of lung transplantation.

Types of comparison

Because of the paucity of evidence, all intervention comparisons were assessed but meta-analysis was only conducted for randomised controlled trials (RCTs) of placebo-controlled interventions.

Types of outcome measures

The outcomes included were effects on dyspnoea (at rest), QoL, all other symptoms, 6-minute walking distance (6MWD) and economic data.

Types of study included

A scoping search identified a paucity of controlled trials so all trials, including prospective and retrospective studies, were evaluated. Studies published only in abstract form were included if sufficient information was available to satisfy inclusion criteria. Higher weighting was given to randomised placebo-controlled studies. The quality of RCTs was assessed as described by Jadad *et al.*⁴ Studies with qualitative enquiry or mixed method designs were also included. Studies with fewer than five patients were excluded. Paediatric studies were excluded due to radical differences in the PIF-ILD syndromes between childhood and adulthood.⁵

Data extraction

Details of data extraction can be found in online appendix 1.

Data analysis

Where data quantity and quality allowed, data were combined using fixed or random effects meta-analysis. The choice of model was determined by the degree of heterogeneity, as judged by the I^2 statistic and p value for the χ^2 test (a random effects model was used if $p < 0.10$ and/or $I^2 > 50\%$). Results are presented as pooled mean differences between intervention and placebo groups with 95% CI. Forest plots are used to display the results from the individual studies and the pooled estimate. For single studies, the effect size and 95% CI were calculated using standard formulae when not reported in the original paper. A descriptive summary of other studies has been given.

RESULTS

Overview of included studies

Joint data extraction was conducted for 75 papers with interventional data (figure 1). Thirty-four papers were included (see online appendix 2) and 41 were excluded or listed as potentially relevant (see online appendix 3). Of the 34 papers included, these reported 35 studies (two papers each contained two studies^{6 7} and one study was reported in two papers^{8 9}). No health economic papers were identified.

Seventeen pharmacological interventions and two non-drug interventions were evaluated. In total, 3635 patients were used in the analysis (IPE, $n=3419$; CEA, $n=153$; IIP, $n=54$; usual interstitial pneumonia (UIP), $n=9$) with a range of 6–826. Interferon γ -1b (IFN γ -1b) was the intervention most tested, with the greatest number of patients analysed, the greatest number of RCTs and the largest individual RCT. Pulmonary rehabilitation had the largest number of studies ($n=6$).^{10 15}

The 17 RCTs had an average Jadad score of 4 (range 2–5). There was a preponderance of placebo-controlled RCTs with few comparisons across classes (notably between pharmacological and non-pharmacological interventions). Twenty-six studies used American Thoracic Society/European Respiratory Society (ATS/ERS) diagnostic criteria.¹⁶ Only two papers were not published in English.^{13 17}

Studies were funded by industry (20%), industry and other sources (6%), government (6%), investigators (3%) and other sources such as charities (31%), with the funding source unclear in (34%).

Outcome measures

There were a wide range of outcome measures for dyspnoea and QoL (table 1, see appendix 4).

Interventions

Interventions are presented in order of weighted evidence by study design and subdivided into 6MWD, dyspnoea and other symptoms and QoL. Evidence supported by meta-analysis is listed as 'strong', if supported by single RCTs the evidence is listed as 'moderate'. All other evidence which is supported by non-RCT study designs has been listed as 'weak'. A summary of the results are presented in table 2 and effect sizes are shown in table 3 with full results in appendix 2.

Interventions trialled in RCTs

Interferon γ -1b (IFN γ -1b)

6MWD, dyspnoea and cough: Three RCTs^{23 25 32} studied IFN γ -1b in 908 patients. There were no significant effects of IFN γ -1b on 6MWD (figure 2), dyspnoea (figure 3) or cough.

QoL: There was a significant difference in St George's Respiratory Questionnaire (SGRQ) symptom domain favouring IFN in one study (change in mean score from baseline: IFN -13.2 (95% CI -21.4 to 5.0) vs colchicine 7.5 (95% CI -4.5 to 19.5), $p=0.01$).²³ However, no other improvements in QoL were seen.

Sildenafil

Sildenafil was trialled in four studies, two RCTs^{6 21} (one of which⁶ which was followed by an open-label study) and an uncontrolled quasi-experimental study.²⁰ A total of 378 patients were used in the analysis.

6MWD: Collard *et al.*²⁰ conducted an open-label uncontrolled quasi-experimental study which found a significant mean improvement in 6MWD of 49.0 m (95% CI 17.5 to 84.0). Eleven patients were used in the analysis. However, a

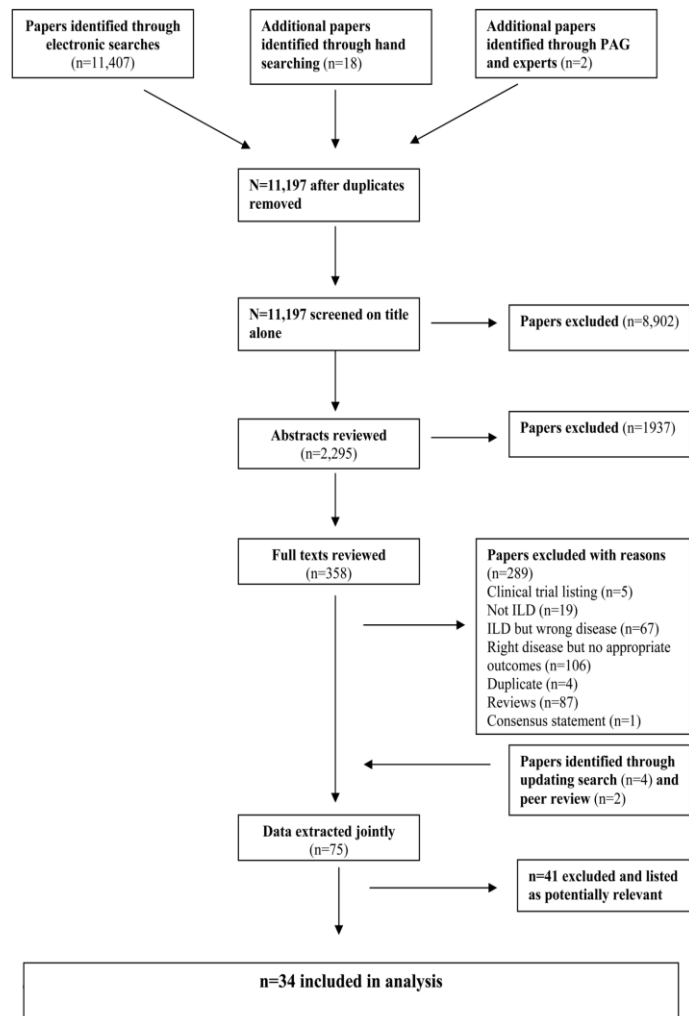


Figure 1 Flow of studies through review.

meta-analysis of data from the two larger RCTs^{6 21} did not support this finding (figure 4).

Dyspnoea: One RCT⁶ showed less deterioration in dyspnoea but overall benefit was not supported by meta-analysis (figure 5).

QoL: Zisman *et al*⁶ found that the SGRQ total score remained stable in the sildenafil group but worsened in the placebo group (mean difference -4.08 (95% CI -7.3 to -0.86)). The Short Form Health Survey (SF-36) general health subscore was better preserved in the sildenafil group than in the placebo group (mean difference 2.86 (95% CI 0.76 to 4.95)). This was not seen during the open-label phase.

Pulmonary rehabilitation

Six studies used pulmonary rehabilitation as the intervention. These included two RCTs^{10 11} and four quasi-experimental open-label studies,^{12 14 15} of which two had controls. A total of 194 patients were used in the analysis.

6MWD: Meta-analysis showed an overall significant benefit of pulmonary rehabilitation on 6MWD (figure 6). This was also supported by other non-randomised studies.^{12 14 15}

Dyspnoea and other symptoms: Nishiyama *et al*¹⁰ found no significant effects on dyspnoea. However, in a subset of patients in the paper by Holland *et al*,¹¹ even though improvements were not seen in the MRC scale, a positive effect was seen for the Chronic Respiratory Disease Questionnaire (CRDQ) dyspnoea score. Kozu *et al*¹⁴ also found a significant improvement in dyspnoea in the IPF subgroup ($p < 0.01$). Ozalevli *et al*¹² found a significant decrease in baseline MRC score after pulmonary rehabilitation ($p = 0.003$) and Rammaert *et al*¹³ found non-significant changes in the Borg and MRC scales. Swigris *et al*¹⁵ found that there was a significant improvement in fatigue. There were no significant improvements in anxiety, depression or sleep quality.

QoL: Two RCTs^{10 11} found positive effects on QoL in a number of domains of the SF-36, CRDQ and SGRQ, of which

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Table 1 Outcome measures used in studies analysed

Type of outcome measure	Symptom	Outcome measure	Papers using outcome measure
Symptom control	Dyspnoea	Borg Dyspnoea Index	Krowka <i>et al.</i> ¹⁸ Ozalevli <i>et al.</i> ¹² Zisman <i>et al.</i> ⁶ Hicks <i>et al.</i> ¹⁹ Collard <i>et al.</i> ²⁰ King Jr <i>et al.</i> ⁸ Raghu <i>et al.</i> ⁹ Rammaert <i>et al.</i> ¹³ Jackson <i>et al.</i> ²¹ Visca <i>et al.</i> ²²
		Medical Research Council Scale	Antoniou <i>et al.</i> ²³ Holland <i>et al.</i> ¹¹ Ozalevli <i>et al.</i> ¹² Varney <i>et al.</i> ²⁴ Rammaert <i>et al.</i> ¹³ Kozu <i>et al.</i> ¹⁴ Strieter <i>et al.</i> ²⁵
		Baseline Dyspnoea Index	Nishiyama <i>et al.</i> ¹⁰ King <i>et al.</i> ²⁶ King Jr <i>et al.</i> ⁸ Raghu <i>et al.</i> ⁹ Strieter <i>et al.</i> ²⁵ Rammaert <i>et al.</i> ¹³ Kozu <i>et al.</i> ¹⁴
		Transition Dyspnoea Index	King <i>et al.</i> ²⁶ King Jr <i>et al.</i> ⁸ Raghu <i>et al.</i> ⁹ Strieter <i>et al.</i> ²⁵ Kozu <i>et al.</i> ¹⁴
		Visual Analogue Scale	Rammaert <i>et al.</i> ¹³ Allen <i>et al.</i> ²⁷
		Four-step improvement in dyspnoea scale	Turner-Warwick <i>et al.</i> ²⁸
		Five-point dyspnoea scale	Agusti <i>et al.</i> ²⁹
		20-point dyspnoea scale	Fiorucci <i>et al.</i> ³⁰ Demedts <i>et al.</i> ³¹ Undurraga <i>et al.</i> ¹⁷
		University of California San Diego Scale	Zisman <i>et al.</i> ⁶ King <i>et al.</i> ³² Lindell <i>et al.</i> ³³ Strieter <i>et al.</i> ²⁵ Noble <i>et al.</i> ⁷
		NYHA	Krowka <i>et al.</i> ¹⁸
	Cough	Mahler Dyspnoea Scale	Hanania and Thomas ³⁴
		Visual Analogue Scale	Raghu <i>et al.</i> ³⁵
		Leicester Cough Questionnaire	Hope-Gill <i>et al.</i> ³⁶
		Question 2 on St George's Respiratory Questionnaire	Lutherer <i>et al.</i> ³⁷ Horton <i>et al.</i> ³⁸
	Depression	Dry, productive or absent	Antoniou <i>et al.</i> ²³
		HADS	Rammaert <i>et al.</i> ¹³
	Anxiety	Beck Depression	Lindell <i>et al.</i> ³³
		Patient Health Questionnaire-8	Swigris <i>et al.</i> ¹⁵
	Fatigue	Beck Anxiety	Lindell <i>et al.</i> ³³
		General Anxiety Disorder-7	Swigris <i>et al.</i> ¹⁵
Quality of life	Sleep	Fatigue severity scale	Swigris <i>et al.</i> ¹⁵
		Pittsburgh Sleep Quality Index	Swigris <i>et al.</i> ¹⁵
	SF-36	SF-36	Holland <i>et al.</i> ¹¹ King <i>et al.</i> ²⁶ Zisman <i>et al.</i> ⁶ King Jr <i>et al.</i> ⁸ Raghu <i>et al.</i> ⁹ Raghu <i>et al.</i> ³⁵ Rammaert <i>et al.</i> ¹³ Swigris <i>et al.</i> ¹⁵
		SF-36 Japanese version	Kozu <i>et al.</i> ¹⁴ Tomioka <i>et al.</i> ³⁹
		SF-36 Turkish version	Ozalevli <i>et al.</i> ¹²
		St George's Respiratory Questionnaire	Nishiyama <i>et al.</i> ¹⁰ Antoniou <i>et al.</i> ²³ Varney <i>et al.</i> ²⁴ Zisman <i>et al.</i> ⁶ King <i>et al.</i> ³² King Jr <i>et al.</i> ⁸
		EQoD	Raghu <i>et al.</i> ⁹ Demedts <i>et al.</i> ³¹ Raghu <i>et al.</i> ³⁵ Rammaert <i>et al.</i> ¹³ Mishra <i>et al.</i> ⁴⁰
		Chronic Respiratory Disease Questionnaire	King <i>et al.</i> ²⁶ Zisman <i>et al.</i> ⁶
			Holland <i>et al.</i> ¹¹

the SGRQ total score was also significant ($p < 0.05$). This was supported by Ozalevli *et al.*¹² and Rammaert *et al.*¹³ who found that, among other positive QoL results, SF-36 physical limitation scores decreased significantly post-intervention ($p = 0.05$).¹³ Other non-randomised studies did not find any positive effects on QoL.^{14 15}

Bosentan

Two RCTs were reported in three papers trialling bosentan,^{8 9 26} with 769 patients included in the analysis.

6MWD: BUILD-1 showed no benefit of bosentan compared with placebo for 6MWD.^{8 9}

Dyspnoea: In BUILD-1 there was no significant effect of bosentan on dyspnoea in the total population or in the diagnostic biopsy subset at the primary endpoint of 12 months.^{8 9} These findings were supported by a second larger RCT (BUILD-3).²⁶

QoL: BUILD-1 found no difference for any domain of the SGRQ at 12 months.⁸ Forty-two percent of bosentan-treated patients had an improved SF-36 health transition score compared with 28% of the placebo group ($p = 0.084$). However, a subanalysis of patients who had undergone diagnostic biopsy favoured bosentan, showing a significant beneficial effect on QoL with mean total SGRQ scores favouring bosentan.⁸ Significant treatment effects were observed at 12 months in the impact domain of the SGRQ (median treatment effect (MTE) -7.0 , $p = 0.03$) and the physical functioning (MTE 9.3 , $p = 0.04$), general health (MTE 9.4 , $p = 0.01$) and role emotional domains

of the SF-36 (MTE 0.0 , $p = 0.04$).⁹ However, none of these findings were supported in the larger BUILD-3 study.²⁶

Pirfenidone

Two RCTs (CAPACITY) testing pirfenidone were presented in one paper.⁷ A total of 692 patients were included in the analysis. Significant improvement was seen in 6MWD of pooled data for the intervention group compared with placebo (absolute difference 24.0 m (95% CI 4.3 to 43.7)). No significant change in dyspnoea score was seen (table 3) and there were no QoL data.

N-acetylcysteine (NAC)

Two RCTs^{39 41} with 177 patients included in the analysis did not show any significant differences for aerosolised or oral NAC compared with control for 6MWD, dyspnoea or QoL.

Co-trimoxazole

A pilot RCT of 20 patients compared oral co-trimoxazole alone with a combination with oral prednisolone.²⁴

Dyspnoea and other symptoms: The MRC dyspnoea score showed improvement with a median score of 3 (95% CI 2 to 4) before treatment compared with 2 (95% CI 1 to 3) 3 months after treatment for the active group ($p = 0.05$) which was maintained at 12 months. The Borg breathlessness score and visual analogue scale (VAS) score were significantly improved (data not presented in paper). Cough improved within 4 weeks of treatment ($p = 0.002$) (data not presented in paper).

Table 2 Summary of studies included and results (presented as radical or palliative treatments and in order of weighted evidence)

Intervention	Papers	Patients analysed	Disease group with diagnostic criteria	Type of trial with Jadad score if applicable	Control	Summary of results
Radical treatments						
IFN- γ -1b	King <i>et al</i> ²² Antoniou <i>et al</i> ²³ Strieter <i>et al</i> ²⁵	826 50 32	IPF: ATS/ERS IPF: ATS/ERS IPF: ATS/ERS	RCT (5) RCT (3) RCT (3)	Placebo two-arm colchicine and IFN placebo	No significant effects of IFN- γ -1b on 6MWD, dyspnoea and cough. Significant difference in SGRQ symptom domain in one study. No other improvement in QoL seen
Sildenafil	Four studies, three papers and three cohorts of patients; Zisman <i>et al</i> ⁶ Jackson <i>et al</i> ²¹ Collard <i>et al</i> ²³	180 161 cont 26 11	IPF: ATS/ERS IPF: ATS/ERS IPF: ATS/ERS	RCT (5) Quasi-experimental open-label RCT (5) Quasi-experimental open-label	Placebo two-arm sildenafil Placebo No control	Improvement in smaller open-label uncontrolled study of 6MWD which is not supported by RCTs. Less deterioration of dyspnoea in intervention group compared with placebo of one RCT which is not supported by meta-analysis. Some preservation of QoL scores for sildenafil compared with placebo found in RCT
Bosentan	King Jr <i>et al</i> (BUILD-1) ⁸ Raghu <i>et al</i> (2nd paper BUILD-1) ⁹ King <i>et al</i> ²⁶	154 615	IPF: ATS/ERS IPF: ATS/ERS	RCT (3) RCT (5)	Placebo Placebo	No effects on 6MWD or dyspnoea at rest seen. Minimal QoL changes in all treated population; some more marked benefits in subgroup with biopsies was seen in BUILD-1 but these were not supported by the larger BUILD-3 study
Pirfenidone	Noble <i>et al</i> ⁷ (CAPACITY trial 004) Noble <i>et al</i> ⁷ (CAPACITY trial 006)	348 344	IPF: ATS/ERS IPF: ATS/ERS	RCT (5) RCT (5)	Placebo Placebo	Positive effect on 6MWD. No significant effect on dyspnoea. No QoL data
NAC	Tomioka <i>et al</i> ²⁹ Demedts <i>et al</i> ³¹	22 155	IPF: ATS/ERS IPF: ATS/ERS	RCT (3) RCT (4)	Bromohexine Placebo	No evidence for NAC improving 6MWD, dyspnoea or QoL
Co-trimoxazole	Vamey <i>et al</i> ²⁴	20	IIP:ATS/ERS	RCT (5)	Placebo	Some improvements in dyspnoea and SGRQ symptom score but numbers small
Etanercept	Raghu <i>et al</i> ³⁵	87	IPF: ATS/ERS	RCT (3)	Placebo	No evidence for etanercept improving 6MWD, dyspnoea or QoL
Iloprost	Krowka <i>et al</i> ¹⁸	51	IPF: no criteria given	RCT (3)	Matched placebo	No evidence for iloprost improving 6MWD, dyspnoea or QoL
D-pencillamine	Hanania <i>et al</i> ³⁴	10	IPF: no criteria given	Quasi-experimental, open-label	No control	Improvement in dyspnoea following administration of D-pencillamine but weak study design and numbers small
Interferon α	Lutherer <i>et al</i> ³⁷	6	IPF: ATS/ERS	Quasi-experimental, open-label	No control	Improvement in cough following administration of interferon α lozenges but weak study design and numbers small
Ribavarin	Agusti ²⁹	10	CFA: Turner Warwick	Quasi-experimental, open-label	No control	No improvement in dyspnoea following administration of aerosolised ribavirin
Colchicine	Undurraga <i>et al</i> ¹⁷	17	IPF: Turner Warwick criteria	Quasi-experimental, open-label	No control	Improvement in dyspnoea following administration of colchicine but weak study design and numbers small
Doxycycline	Mishra <i>et al</i> ⁴⁰	6	IPF: ATS/ERS	Quasi-experimental, open-label	No control	No improvement in 6MWD following administration of doxycycline. Improvement in QoL but weak study design and numbers very small
Prednisolone*	Hope-Gill <i>et al</i> ³⁶ Turner-Warwick <i>et al</i> ²⁸ Fiorucci <i>et al</i> ³⁰	6 127 30	IPF: ATS/ERS CFA: Turner-Warwick IPF: ATS/ERS	Quasi-experimental, open-label Retrospective case note review Quasi-experimental, open-label	No control No control Three arms: colchicine, cyclophosphamide and prednisolone	Some improvement in dyspnoea in prednisolone groups but numbers small and weak study design
Palliative treatments						
Pulmonary rehabilitation	Holland <i>et al</i> ¹¹ Nishiyama <i>et al</i> ¹⁰ Ozalevi <i>et al</i> ¹²	34 28 15	IPF: ATS/ERS IPF: ATS/ERS IPF: ATS/ERS	RCT (3) RCT (3) Quasi-experimental, open-label	Telephone advice Usual care No control	6MWD improved immediately following pulmonary rehabilitation (however not as much as in COPD). Mixed results for dyspnoea. Positive effects on fatigue and QoL also seen

Continued

Review

Table 2 Continued

Intervention	Papers	Patients analysed	Disease group with diagnostic criteria	Type of trial with Jadad score if applicable	Control	Summary of results
Disease management programme	Rammar et al ¹³	13	IPF/ATS/ERS	Quasi-experimental, open-label	No control	Mixed evidence on benefit of disease management programme in improving symptoms and QoL. Quantitative work suggested negative impact of intervention on perceptions of physical QoL and a tendency for greater anxiety. Qualitative work suggested patients felt less isolated and were able to put their disease into perspective
	Kozu et al ¹⁴	90	IPF/ATS/ERS	Quasi-experimental, open-label	COPD group	
	Swigons et al ¹⁵	14	IPF/ATS/ERS	Quasi-experimental, open-label	COPD group	
	Lindell et al ¹⁶	21	IPF: unclear	RCT (2) with qualitative interviews	Usual care	
Oxygen	Hicks et al ¹⁹	70	IPF: ATS/ERS	Retrospective case note study	Two-arm oxygen	Improvement in 6MWD and some improvements in dyspnoea in oxygen-treated groups, but weak study designs
Diamorphine	Visca et al ²²	34	IPF/NSIP: ATS/ERS	Retrospective case note study	No control	
	Allen et al ²⁷	11	IPF: characteristic changes on chest x-ray	Quasi-experimental, open-label	No control	
Thalidomide	Horton et al ²⁸	11	IPF: ATS/ERS	Quasi-experimental, open-label	No control	Improvement in cough and QoL related to cough following administration of thalidomide but weak study design and numbers small

*May be considered both a radical and palliative treatment. ATS, American Thoracic Society; CFA, cryptogenic fibrosing alveolitis; Cont, patients continuing into open label phase; COPD, chronic obstructive pulmonary disease; ERS, European Respiratory Society; IFN, interferon; IPF, idiopathic pulmonary fibrosis; 6MWD, 6-minute walking distance; NAC, N-acetylcysteine; NSIP, non-specific interstitial pneumonia; QoL, quality of life; RCT, randomised controlled trial.

QoL: The SGRQ showed a significant reduction in symptom scores in the co-trimazole group ($p=0.05$) but an improvement was also seen in the placebo group ($p=0.02$). Non-significant effect sizes were seen for other components of the SGRQ.

Etanercept

A RCT of etanercept in 87 patients with IPF showed no significant improvement in 6MWD (table 3), dyspnoea or QoL compared with placebo (data not presented in paper).³⁵

Iloprost

A RCT of 51 patients treated with inhaled iloprost showed no significant differences between inhaled iloprost and placebo for change in 6MWD or Borg dyspnoea score (data not presented in paper).¹⁸

Disease management programme

Lindell et al¹⁶ conducted a RCT of 21 patients which compared a disease management programme delivered using a format of support group for both patients with IPF and carers with a control group of best usual care. There was mixed evidence of benefit.

Quantitative work suggested a negative impact of this intervention on perceptions of physical QoL and a tendency for greater anxiety. The mean end Beck Anxiety Index scores approached statistical significance (intervention 15.13 (6.92) vs control 8.56 (6.95), $p=0.077$), reflecting increased anxiety in the intervention group. The mean (SD) end score for the SF-36 physical component showed a statistically significant difference (intervention 31.06 (4.61) vs control 36.04 (4.63), $p=0.038$), reflecting a negative impact on perceptions of physical health-related QoL. However, qualitative work in which 19 participants in the experimental group were interviewed found that patients did not feel isolated and felt that the intervention had enabled them to put the disease into perspective, gave comfort and provided an improved mental picture.

Interventions trialled more than once in non-randomised controlled studies*Prednisolone*

Two quasi-experimental studies^{30 36} and one retrospective review²⁸ were included. A total of 163 patients were used in the analysis.

Dyspnoea and other symptoms: Fiorucci et al³⁰ conducted a three-arm study of 30 patients using prednisolone alone (group 1), prednisolone and cyclophosphamide (group 2) and prednisolone and colchicine (group 3). There were significant improvements in dyspnoea in the prednisolone and colchicine group compared with the two other groups (mean (SD) baseline dyspnoea score 8.4 (2.5) vs 6.3 (2.2) at 18 months ($p=0.001$)). Two patients in group 1 (18%), one patient in group 2 (11%) and eight patients in group 3 (80%) showed a significant decrease in dyspnoea ($p=0.001$). However, the numbers were small and the study was conducted in a single centre. Turner Warwick et al²⁸ conducted a retrospective review which included 127 patients in the analysis. After 4–6 weeks of treatment, 55 (43%) were classified as non-responders and 72 (57%) as responders with improvement in dyspnoea on a 4-point scale. However, patients were classed as CFA using the criteria of Turner Warwick et al⁴¹ without diagnostic biopsies.

Hope-Gill et al³⁶ conducted an open-label study of prednisolone on capsaicin-induced cough and found a significant reduction in cough reflex sensitivity to capsaicin with a reduction in the mean (SE) VAS score from 7.2 (0.8) to 2.2 (2.5) at 4 weeks ($p<0.05$). However, the numbers were small ($n=6$) and only five of the six patients reported VAS data.

Table 3 Effect sizes and pooled estimates where applicable

Interventions ordered by evidence	Study	Outcome	Change from baseline, mean difference (95% CI)	Effect size, mean difference (95% CI)	Pooled estimate (95% CI), I^2 and p value if applicable
Interferon γ -1b	King <i>et al</i> ⁸²	6MWD		-7.80 (-31.8 to 15.9)	-7.45 (-30.26 to 15.36), $I^2=0.0\%$, $p=0.52$
	Strieter <i>et al</i> ²⁵			-3.20 (-85.7 to 79.3)	
	King <i>et al</i> ⁸²	UCSD		0.40 (-4.1 to 4.87)	0.08 (-4.18 to 4.34), $I^2=0.0\%$, $p=0.97$
	Strieter <i>et al</i> ²⁵			-3.1 (-17.19 to 11.01)	
	King <i>et al</i> ⁸²	SGRQ total score		-0.50 (-2.53 to 1.53)	
Sildenafil	Zisman <i>et al</i> ⁶	6MWD		16.7 (-3.92 to 37.32)	5.25 (-8.90 to 19.40), $I^2=56.6\%$, $p=0.47$
	Jackson <i>et al</i> ²¹	6MWD		0.70 (-0.43 to 1.83)	
	Zisman <i>et al</i> ⁶	Borg		-0.34 (-0.81 to 0.14)	-0.34 (-0.82 to 0.13), $I^2=39.5\%$, $p=0.16$
	Jackson <i>et al</i> ²¹	Borg		-31.0 (-77.73 to 15.73)	
	Zisman <i>et al</i> ⁶	UCSD		-6.58 (-11.25 to -1.92)	
		SGRQ total score		-4.08 (-7.3 to -0.86)	
		SGRQ symptom score		-5.73(-10.61 to -0.85)	
		SGRQ activity score		-3.64 (-7.2 to -0.09)	
		SGRQ impact score		-3.7 (-7.76 to 0.37)	
		SF-36 aggregate physical score		-0.17 (-2.06 to 1.73)	
		SF-36 aggregate mental score		-1.72 (-4.38 to 0.94)	
		SF-36 aggregate bodily pain score		-2.17 (-4.86 to 0.52)	
		SF-36 general health score		2.86 (0.76 to 4.95)	
		SF-36 mental health score		1.15 (-1.15 to 3.46)	
		SF-36 physical functioning		0.53 (-1.31 to 2.37)	
		SF-36 role emotional score		2.1 (-1.9 to 6.1)	
		SF-36 role physical score		1.16 (-1.62 to 3.93)	
		SF-36 social functioning		1.99 (-1.22 to 5.21)	
		Vitality score difference		2.03 (-0.39 to 4.44)	
		EuroQol		0.02 (-0.04 to 0.08)	
		EuroQol thermometer		2.28 (-2.75 to 7.32)	
Pulmonary rehabilitation	Nishiyama <i>et al</i> ¹⁰	6MWD		46.30 (8.30 to 84.40)	27.4 (4.1 to 50.7), $I^2=33.9\%$, $p=0.021$
	Holland <i>et al</i> ¹¹			16.12 (-13.32 to 45.56)	
	Kozu <i>et al</i> ¹⁴		16.2 (7.1 to 25.4)		
	Holland 2008	SF-36 functioning		1.83 (-1.19 to 4.85)	
	Kozu <i>et al</i> ¹⁴		1.9 (-1.1 to 5)		
	Holland 2008	SF-36 role physical		1.01 (0.27 to 1.75)	
	Kozu <i>et al</i> ¹⁴		1.0 (-1.6 to 3.6)		
	Holland 2008	SF-36 pain index		0.69 (-0.95 to 2.33)	
	Kozu <i>et al</i> ¹⁴		-2.7 (-8.2 to 2.7)		
	Holland <i>et al</i> ¹¹	SF-36 general health perception		2.67 (0.23 to 5.09)	
	Kozu <i>et al</i> ¹⁴		-0.2 (-2.8 to 2.4)		
	Holland <i>et al</i> ¹¹	SF-36 vitality		4.50 (2.24 to 6.76)	
	Kozu <i>et al</i> ¹⁴		0.9 (-1.9 to 3.6)		
	Holland <i>et al</i> ¹¹	SF-36 social functioning		1.73 (-0.05 to 3.51)	
	Kozu <i>et al</i> ¹⁴		-0.7 (-3.2 to 1.8)		
	Holland <i>et al</i> ¹¹	SF-36 role emotional		0.10 (-0.90 to 1.10)	
	Kozu <i>et al</i> ¹⁴		-0.9 (-5.4 to 3.6)		
	Holland <i>et al</i> ¹¹	SF-36 mental health index		4.52 (1.10 to 7.94)	
	Kozu <i>et al</i> ¹⁴		1.9 (-1.1 to 5)		

Continued

Review

Table 3 Continued

Interventions ordered by evidence	Study	Outcome	Change from baseline, mean difference (95% CI)	Effect size, mean difference (95% CI)	Pooled estimate (95% CI), I ² and p value if applicable
	Holland <i>et al</i> ¹¹	MRC scale		−0.84 (−1.73 to 0.05)	
	Kozu <i>et al</i> ¹⁴		−0.4 (−0.6 to −0.3)		
	Nishiyama <i>et al</i> ¹⁰	Baseline Dyspnoea Index		0.4 (−0.6 to 1.4)	
		SGRQ total score		−6.1 (−11.7 to −0.5)	
		SGRQ symptom score		−5.7 (−18.7 to 7.2)	
		SGRQ activity score		−5.8 (−14.7 to 3.1)	
		SGRQ impact score		−6.2 (−12.8 to 0.3)	
	Holland <i>et al</i> ¹¹	CRDQ dyspnoea		5.43 (1.34 to 9.52)	
		CRDQ fatigue		4.67 (1.76 to 7.58)	
		CRDQ mastery		3.33 (0.82 to 5.84)	
		CRDQ emotional		7.44 (0.87 to 14.01)	
	Swigris <i>et al</i> ¹⁵	6MWD	61.6 (−19.08 to 142.22)		
		Fatigue Severity Scale	−1.5 (−2.48 to −0.52)		
		General Anxiety Disorder 7	−1.4 (−3.36 to 0.56)		
		Patients' Health Questionnaire 8	−0.9 (−2.27 to 0.47)		
		Pittsburgh Sleep Total	0.9 (−0.67 to 2.47)		
		SF-36 physical functioning	1.2 (−3.11 to 5.51)		
		Role physical	1.5 (−2.42 to 5.42)		
		Bodily pain	2.7 (−2.59 to 7.99)		
		General health	1.4 (−4.09 to 6.89)		
		Vitality	3.6 (−0.71 to 7.91)		
		Social functioning	1.9 (−2.41 to 6.21)		
		Role emotional	−1.9 (−10.33 to 6.53)		
		Mental health	1.6 (−1.73 to 4.93)		
		Physical component summary	3.0 (−1.12 to 7.12)		
		Mental component summary	0.3 (−5.19 to 5.79)		
Bosentan	King <i>et al</i> ¹⁶	SF-36 physical functioning		0 (−3.9 to 3.9)	
		SF-36 role-physical		−2.80 (−7.70 to 2.20)	
		SF-36 pain index		0.70 (−4.20 to 5.70)	
		SF-36 general health perception		−2.90 (−6.50 to 0.60)	
		SF-36 vitality		−1.60 (−5.40 to 2.10)	
		SF-36 social functioning		−1.50 (−6.40 to 3.40)	
		SF-36 role-emotional		−3.20 (−8.60 to 2.20)	
		SF-36 mental health index		−1.60 (−5.30 to 2.20)	
		SF-36 health transition score		0 (−0.20 to 0.20)	
		EuroQol EQ-5D health state score		−0.04 (−0.10 to 0.03)	
		EuroQol EQ-5D visual analogue score		−1.50 (−5.40 to 2.40)	
		Transition dyspnoea Index		0.10 (−0.50 to 0.70)	
	King Jr <i>et al</i> ¹⁶	6MWD		−18.00 (−57.23 to 21.23)	
		SGRQ total		−6.60 (−0.72 to −12.48)	
Pirfenidone	Noble <i>et al</i> ⁷	6MWD			24.0 (4.3 to 43.7)
		CAPACITY 004		16.4 (−10.9 to 43.7)	
		CAPACITY 006		31.8 (3.2 to 60.4)	
	CAPACITY 004	UCSD		−3.1 (8.5 to 2.3)	−2.5 (−6.4 to 1.4)
		CAPACITY 006		−2.0 (−7.6 to 3.6)	

Continued

Table 3 Continued

Interventions ordered by evidence	Study	Outcome	Change from baseline, mean difference (95% CI)	Effect size, mean difference (95% CI)	Pooled estimate (95% CI), I ² and p value if applicable
Co-trimoxazole	Varney <i>et al</i> ²⁴	SGRQ total score		-2.52 (-19.01 to 13.97)	
		SGRQ symptom score		-7.5 (-28.54 to 13.54)	
		SGRQ activity score		0.4 (-18.53 to 19.33)	
		SGRQ impact score		-5.9 (-24.21 to 12.41)	
Etanercept	Raghu <i>et al</i> ²⁵	6MWD		14.9 (-29.28 to 59.08)	
NAC	Tomioka <i>et al</i> ²⁹	6MWD		66.4 (-37.94 to 170.74)	
		SF-36 physical functioning		-0.7 (-18.18 to 16.78)	
		SF-36 bodily pain		-6.1 (-30.52 to 18.32)	
		SF-36 role physical		-6.7 (-42.77 to 29.38)	
		SF-36 general health		6.4 (-6.36 to 19.16)	
		SF-36 vitality		13.4 (-1.45 to 28.25)	
		SF-36 social functioning		8.7 (-11.27 to 28.68)	
		SF-36 role emotional		42.2 (-1.64 to 86.04)	
		SF-36 mental health		12.7 (0.76 to 26.16)	
	Demedts <i>et al</i> ³¹	Dyspnoea score		-0.32 (-1.72 to 1.09)	
Interferon α	Lutherer <i>et al</i> ²⁷	Leicester cough questionnaire score	3.16 (1.58 to 4.74)		
Doxycycline	Mishra <i>et al</i> ⁴⁰	6MWD	43.0 (-36.05 to 122.01)		
		Total SGRQ score	-32.5 (22.91 to 42.09)		

Lower SGRQ score indicates better quality of life. Higher score on EQ-5D indicates a better quality of life and a negative value indicates a health state worse than death. CRDQ, Chronic Respiratory Disease Questionnaire; 6MWD, 6-minute walking distance; NAC, N-acetylcysteine; SF-36, Short Form Health Survey; SGRQ, St George's Respiratory Questionnaire; UCSD, University of California San Diego shortness of breath questionnaire.

Figure 2 Forest plot showing comparison of effect of interferon γ -1b (IFN γ -1b) versus control on change in 6-minute walking distance (6MWD): effect size -7.45 (95% CI -30.26 to 15.36), $p=0.52$.

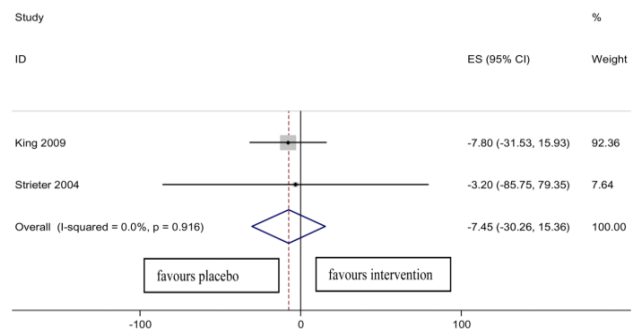


Figure 3 Forest plot showing comparison of effect of interferon γ -1b (IFN γ -1b) versus control on change in San Diego breathlessness scale: effect size 0.08 (95% CI -4.18 to 4.34), $p=0.97$.

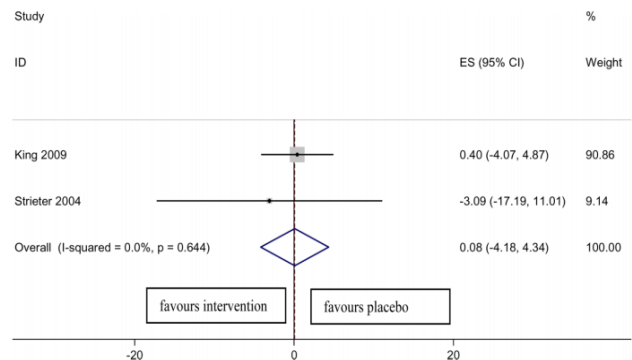


Table 3 Continued

Interventions ordered by evidence	Study	Outcome	Change from baseline, mean difference (95% CI)	Effect size, mean difference (95% CI)	Pooled estimate (95% CI), I ² and p value if applicable
Co-trimoxazole	Vamey <i>et al</i> ²⁴	SGRQ total score		-2.52 (-19.01 to 13.97)	
		SGRQ symptom score		-7.5 (-28.54 to 13.54)	
		SGRQ activity score		0.4 (-18.53 to 19.33)	
		SGRQ impact score		-5.9 (-24.21 to 12.41)	
Etanercept	Raghu <i>et al</i> ²⁵	6MWD		14.9 (-29.28 to 59.08)	
NAC	Tomioka <i>et al</i> ²⁹	6MWD		66.4 (-37.94 to 170.74)	
		SF-36 physical functioning		-0.7 (-18.18 to 16.78)	
		SF-36 bodily pain		-6.1 (-30.52 to 18.32)	
		SF-36 role physical		-6.7 (-42.77 to 29.38)	
		SF-36 general health		6.4 (-6.36 to 19.16)	
		SF-36 vitality		13.4 (-1.45 to 28.25)	
		SF-36 social functioning		8.7 (-11.27 to 28.68)	
		SF-36 role emotional		42.2 (-1.64 to 86.04)	
		SF-36 mental health		12.7 (0.76 to 26.16)	
	Demedts <i>et al</i> ³¹	Dyspnoea score		-0.32 (-1.72 to 1.09)	
Interferon α	Lutherer <i>et al</i> ³⁷	Leicester cough questionnaire score	3.16 (1.58 to 4.74)		
Doxycycline	Mishra <i>et al</i> ⁴⁰	6MWD	43.0 (-36.05 to 122.01)		
		Total SGRQ score	-32.5 (22.91 to 42.09)		

Lower SGRQ score indicates better quality of life. Higher score on EQ-5D indicates a better quality of life and a negative value indicates a health state worse than death. CRDQ, Chronic Respiratory Disease Questionnaire; 6MWD, 6-minute walking distance; NAC, N-acetylcysteine; SF-36, Short Form Health Survey; SGRQ, St George's Respiratory Questionnaire; UCSD, University of California San Diego shortness of breath questionnaire.

Figure 2 Forest plot showing comparison of effect of interferon γ -1b (IFN γ -1b) versus control on change in 6-minute walking distance (6MWD): effect size -7.45 (95% CI -30.26 to 15.36), $p=0.52$.

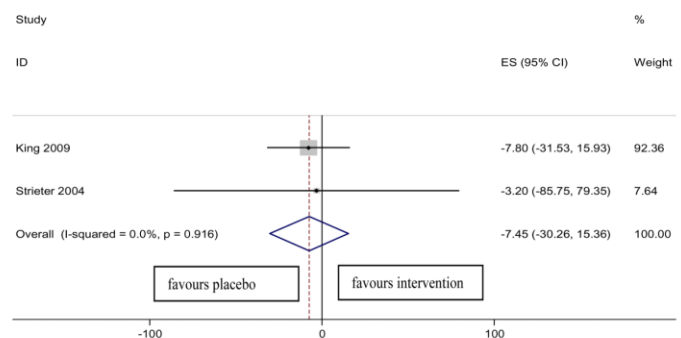
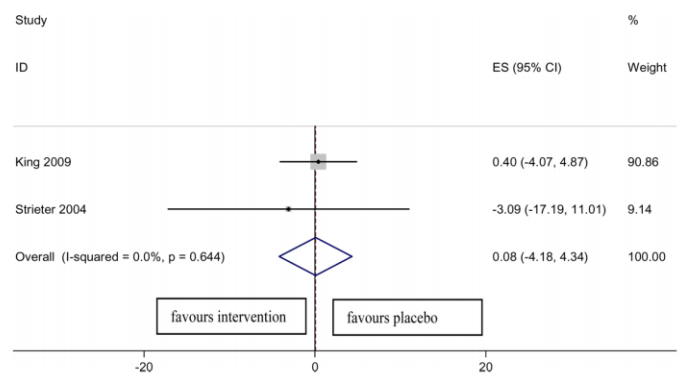
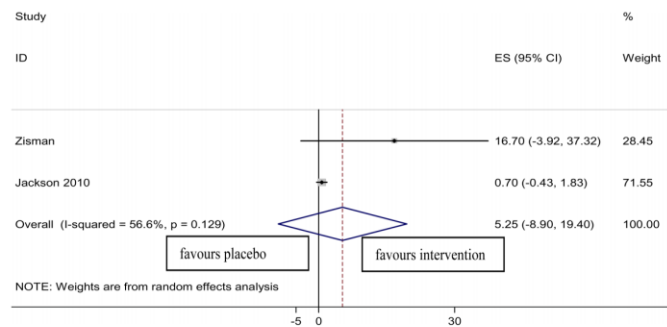


Figure 3 Forest plot showing comparison of effect of interferon γ -1b (IFN γ -1b) versus control on change in San Diego breathlessness scale: effect size 0.08 (95% CI -4.18 to 4.34), $p=0.97$.



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Figure 4 Forest plot showing comparison of effect of sildenafil versus control on change in 6-minute walking distance (6MWD); effect size 5.25 (95% CI -8.90 to 19.40), $p=0.467$.



No 6MWD or QoL data were available for prednisolone.

Oxygen

6MWD: Hicks *et al*¹⁹ conducted a retrospective review of 70 patients with IPF to assess the benefits of ambulatory oxygen. Patients not requiring regular oxygen before the study managed to walk further on optimal oxygen therapy (mean 81.2 m, $p<0.01$). Patients already on regular oxygen showed less benefit on optimal oxygen therapy, walking an extra 16.9 m ($p=0.02$). A second retrospective review²² of 34 patients with IPF/NSIP showed that ambulatory oxygen (additional or increased) significantly improved 6MWD from baseline (mean (SE) 272.3 (19.8) m vs 304.7 (17.8) m, $p=0.0001$).

Dyspnoea: Visca *et al*²² found that dyspnoea measured by the Borg scale improved with oxygen (median 4.25 (95% CI 3 to 5) at baseline vs 3.25 (95% CI 2.5 to 4) on oxygen, $p<0.00001$). Borg scores at the end of the study were not significantly different using optimal oxygen than baseline tests in the study by Hicks *et al*.¹⁹

There were no QoL studies for oxygen.

Interventions trialled only once in non-randomised open-label uncontrolled studies

Diamorphine

An uncontrolled quasi-experimental open-label study²⁷ of 11 patients on subcutaneous diamorphine showed no adverse effects on vital signs and oxygen saturation but a substantial fall in the dyspnoea analogue score from a mean (SD) of 83 (13) at baseline to 36 (11) at 15 min and 36 (12) at 30 min ($p<0.001$). The authors also reported decreased observed anxiety (no details given). However, strict diagnostic criteria were not used.

D-pencillamine

An uncontrolled quasi-experimental open-label study of D-pencillamine in 10 patients with IPF showed improvement by

one full grade on the New York Heart Association (NYHA) dyspnoea scale in 50% of patients.³⁴ No diagnostic criteria were given.

Interferon α

A quasi-experimental open-label study using interferon α lozenges showed improvements in frequency, duration, intensity of daytime cough and improvements in night-time cough.³⁷ Five of six subjects with chronic cough who completed the Leicester Cough Questionnaire improved with a mean change in total score from baseline of 3.16 (95% CI 1.58 to 4.74), where 1.3 is considered to exceed the minimal important difference.

Ribavirin

An uncontrolled quasi-experimental open-label study of 10 patients with ribavirin showed no significant change in dyspnoea.²⁹

Thalidomide

Cough: A phase II trial of the effect of thalidomide on cough in 11 patients with IPF showed marked improvement/resolution of symptoms.³⁸ Three patients who stopped taking thalidomide all experienced return of cough within 2 weeks but, with reinstitution, all three patients again had resolution of the cough.

QoL: SGRQ data showed a significant decrease on question 2 (cough question) between baseline and 3 months (4.9 (0.3) vs 2.2 (1.6), $p=0.03$).

Colchicine

A quasi-experimental open-label uncontrolled study of 17 patients with IPF showed improvement in dyspnoea of 1.7 units (as part of a composite clinical score) in 10 patients (significance not stated).¹⁷ The diagnostic criteria used were those of Turner Warwick *et al*⁴¹ and therefore patients are likely to

Figure 5 Forest plot showing comparison of effect of sildenafil versus control on change in Borg score at rest; effect size -0.34 (95% CI -0.82 to 0.13), $p=0.157$.

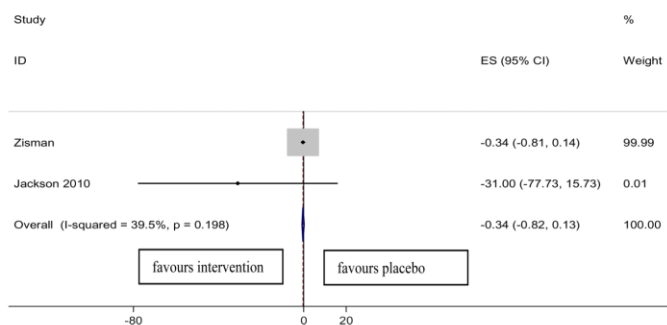
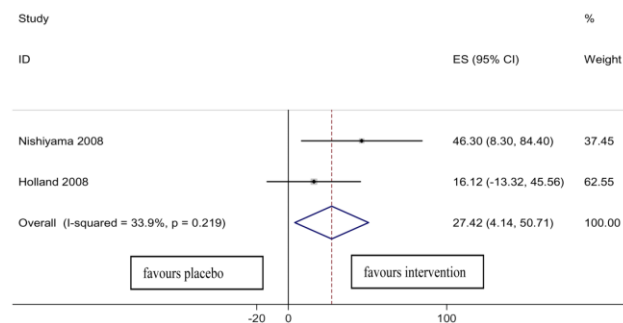


Figure 6 Forest plot showing comparison of effect of pulmonary rehabilitation versus control on change in 6-minute walking distance (6MWD): effect size 27.4 (95% CI 4.1 to 50.7), $p=0.021$.



include a mixed group. Of note, improvement in dyspnoea was also noted in the study by Fiorucci *et al*⁵⁰ which compared colchicine with prednisolone and cyclophosphamide.

Doxycycline

6MWD: A quasi-experimental open-label uncontrolled trial of six patients with IPF showed no improvement in 6MWD.⁴⁰

QoL: There was a significant improvement in QoL on the SGRQ total score after treatment with doxycycline ($p<0.0001$). However, other SGRQ scores were not presented or commented on in the paper.

DISCUSSION

Patients with PIF-ILD suffer a high symptom burden² and impaired QoL³ in the terminal stages of their disease. This systematic review aimed to present the evidence for the use of interventions to improve dyspnoea, other symptoms and QoL in PIF-ILD. We reviewed the symptom scales used in these interventions and sought to perform an economic evaluation of them.

While a recent review examining the treatment of dyspnoea in IPF recommends that sildenafil should be considered,⁴² we do not believe that there is sufficient evidence to support its use in improving dyspnoea. A Cochrane review of physical training for ILD⁴⁵ that involved meta-analyses of RCT evidence for 6MWD, dyspnoea and QoL (and included some unpublished data) supported the use of pulmonary rehabilitation. However, our data, which include all types of studies, can only support the use of pulmonary rehabilitation in improving 6MWD and, to a lesser extent, QoL.

The minimum clinically important difference in 6MWD in patients with IPF has been reported as 24–45 m.^{44–46} Our analysis show that pooled data for both pulmonary rehabilitation and pirfenidone are within that range. Even though pulmonary rehabilitation improved 6MWD, the effect on dyspnoea was mixed. In addition, pirfenidone improved 6MWD but not dyspnoea.⁷ Interplay between functional capacity and dyspnoea at rest is complex and a clear correlation was not found. This may be because dyspnoea is a complex multifaceted problem⁴⁷ which is not necessarily linked to functional capacity, or it may be that appropriate dyspnoea outcome measures were not used.

Although there is weak evidence for ambulatory oxygen, it is worth taking into account that a feature of pulmonary rehabilitation itself is to optimise the use of oxygen prior to proceeding with the programme. Therefore, oxygen may have been an important element of the intervention which adds to its positive effects.

Despite their widespread use, we could find only weak evidence for the benefit of steroids in improving dyspnoea and cough and no extractable or appropriate data on QoL. However, a number of studies were excluded (see appendix 3 online), largely due to mixed patient groups and a paucity of extractable symptom control or QoL data. Individually, it is possible that patients may experience a subjective improvement from a short course of low-dose steroids due to the mood and appetite-enhancing effects. In deciding whether to continue treatment, the subjective symptomatic benefit should be balanced with recent data⁴⁸ and any potential side effect burden.

Our aim in this systematic review was to present the evidence for interventions which improved symptom control and QoL. However, the crucial distinction and essential dichotomy in considering these interventions is to classify them as radical or palliative. In using palliative interventions (eg, diamorphine), the only goal is to improve symptoms and QoL while, in using radical interventions (eg, pirfenidone), the primary goal is to slow disease progression with no adverse effect on symptoms or QoL. When considering the effect of radical treatments, the more important and currently realistic goal may be a stabilisation or slowing in the deterioration of symptoms and QoL. This in itself is important as stabilisation of disease may result in physiological and psychological adaptations which could result in improvement in symptom control and QoL over time.

For patients where radical treatments are being applied, a change in score within a patient group may not be a sensitive measure since the underlying efficacy of the treatment to slow or alter the rate of disease progression may be effective but mirrored by no change in symptom score which would otherwise have declined. For purely palliative interventions, an improvement in symptom experience is often the more meaningful outcome. For example, Zisman *et al*⁶ reported a non-significant change in dyspnoea with sildenafil treatment but presented data showing that there was less deterioration in the intervention group than in the placebo group. Conversely, many other radical interventions do not present these data and a non-significant change cannot be interpreted further. We would encourage authors to present this information clearly to facilitate a true interpretation of the impact of radical interventions on symptoms and QoL.

Our review has highlighted a number of important issues which limit comparison across studies. There was a paucity of RCTs (all were published in the last 10 years), very few studies were powered for QoL or symptoms as the primary outcome, there was poor reporting of data and mixed group studies did not report outcome measures separately. Despite some work at

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developing outcome scales specifically related to this disease group,^{49–51} we found poor use of validated outcome measures and a heterogeneity of measures used. Interestingly, in one study³³ the quantitative results were contradictory to the qualitative results. We would recommend international consensus regarding patient-reported outcome measures and study methodology to ensure that future trials capture accurate symptom control and QoL data. In addition, future trials looking at symptoms and QoL outcomes should include a priori subgroup analysis of patients with severe symptoms and longitudinal analysis of subgroups in which radical interventions result in stable disease.

Patients with IPF experience increased healthcare resource utilisation and direct medical costs.⁵² As the population gets older, we can expect that the burden on healthcare will increase.⁵² We believe that timely and adequate symptom control may prevent unnecessary hospital admissions and therefore contain some expenditure. Interestingly, government funding provided only 6% of support for trials and over a quarter of studies had some source of industry funding. Studies which are funded by industry are unlikely to have symptoms and QoL as primary outcome measures, so the design of these studies may not be best to assess these outcome measures. In the absence of economic analysis of interventions, recommendations about future directions of government spending and conclusions about the resultant potential savings cannot be made.

Study limitations

Only one reviewer retrieved and chose papers. However, a number of sources including a multidisciplinary panel of experts in the ILD and palliative care fields were consulted to ensure that no known studies were missing. We included all study types and all studies regardless of whether PIF-ILD was diagnosed using ATS/ERS criteria.¹⁶ There were only a few studies for each outcome. However, we have only used high-quality studies in the meta-analyses and presented studies clearly to allow readers to draw their own conclusions.

This review presents respiratory physicians with the evidence for interventions in improving 6MWD, dyspnoea, other symptoms and QoL in patients with PIF-ILD.

CONCLUSIONS

There is strong evidence for the use of pulmonary rehabilitation and pirfenidone to improve 6MWD and moderate evidence for the use of sildenafil and pulmonary rehabilitation to improve QoL. The evidence for pulmonary rehabilitation in improving dyspnoea is mixed. There is weak evidence for oxygen, prednisolone, diamorphine, D-penicillamine, colchicine, interferon α , thalidomide and doxycycline which warrants further investigation. Future recommendations for research include consensus on the use of validated outcome scales, primary endpoints related to symptom control and QoL and economic evaluation of interventions. In addition, careful consideration should be given to how symptom control and QoL outcome measures are used and the presentation of data in radical versus palliative treatment contexts.

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Contributors All authors were involved in conceiving the review. SB conducted the review. SB and JRR jointly extracted data. SB and JLP conducted analysis. SB, JRR, JLP and AUW drafted the paper. All authors reviewed a copy of the paper and had intellectual input into the final version.

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Competing interests AUW is a member of the UK Intermune advisory board.

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APPENDIX 1 : Search strategy

We performed comprehensive searches of the following electronic databases:

MEDLINE, EMBASE, Science Citation Index Expanded, pre-MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL) and Database for Abstracts of Reviews of Effectiveness, Health Economic Evaluations Database, LILACS, National Health Service Economic Evaluations Database, AMED and CINAHL from 1966-December 2010 using a combination of MESH headings and keywords. Ongoing trials registers- www.ClinicalTrials.gov and www.who.int/trialsearch were also searched. Furthermore the following websites were also searched: www.cam.org.nz, www.controlledtrials.com, www.rccm.org.uk/ciscom/ CISCOM_intro.aspx and the US food and Drug administration website. Hand searching of journals and conference proceedings for the last 3 years and searching BIOSIS Previews and the Conference Papers Index was conducted. In addition, hand searching of the 3 key respiratory journals THORAX, American Journal of Respiratory and Critical Care Medicine, CHEST for the last 3 years was conducted and of the reference lists of all included papers. The search was updated to September 2011 after all analysis was completed. Study authors were contacted to obtain full reports where abstracts only were available or when further information was required (authors were contacted twice in a month period). No language restrictions were imposed during the searches and translation obtained where needed.

- MEDLINE searched using Ovid interface

Interventions

1. exp idiopathic interstitial pneumonias/ or exp pulmonary fibrosis/
2. (((fibrotic NSIP) or (fibrotic lung disease) or (fibrotic non-specific interstitial pneumonia) or (fibrotic non specific interstitial pneumonia) or (pulmonary fibrosis) or IPF or (cryptogenic fibrosing alveolitis) or (interstitial pneumonia) or UIP or IIP) not cystic fibrosis).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
3. 1 or 2
4. animal/
5. human/
6. 4 not (4 and 5)
7. 3 not 6

Appendix 1 Search strategy

8. (Prednisolone or Methylprednisolone or steroid\$ or corticosteroid\$).mp. or exp prednisolone/ or N-acetylcysteine.mp. or NAC.mp. or acetylcysteine.mp. or exp acetylcysteine/ or azathioprine.mp. or exp azathioprine/ or cyclophosphamide.mp. or exp cyclophosphamide/ or pirfenidone.mp. or exp pyridines/ or interferon gamma 1 b.mp. or IFN.mp. or Interferon-gamma-1b.mp. or IFN-1b.mp. or exp interferon/ or colchicine.mp. or exp colchicine/ or penicillamine.mp. or exp penicillamine/ or exp cyclosporins/ or cyclosporin\$.mp. or Etanercept.mp. or tumor necrosis factor\$.mp. or tumor necrosis factor alpha.mp. or TNF\$.mp. or endothelin-1 antagonist\$.mp. or endothelin 1 antagonist\$.mp. or endothelin antagonist\$.mp. or ET-1 antagonist\$.mp. or ET 1 antagonist\$.mp. or ET receptor antagonist\$.mp. or endothelin receptor antagonist\$.mp. or Bosentan.mp. or exp warfarin/ or Warfarin.mp. or low molecular weight heparin.mp. or LMWH.mp. or exp Heparin/ or exp Heparin, Low-Molecular-Weight/ or Heparin.mp. or lansoprazole.mp. or omeprazole.mp. or exp omeprazole/ or Ranitidine.mp. or histamine H2 receptor antagonist.mp. or exp ranitidine/ or exp proton pump inhibitor/ or proton pump inhibitor.mp. or exp oxygen/ or exp oxygen inhalation therapy/ or O2.mp. or exp oxygen consumption/ or oxygen.mp. or oxygen therapy.mp. or oxygen inhalation therapy.mp. or oxygen consumption.mp. or pharmacological intervention\$.mp. or intervention.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]

9. ((exp nursing/ or exp nursing care/ or nursing.mp. or nursing care.mp. or nursing intervention\$.mp. or exp Physical Therapy Techniques/ or physical therap\$.mp. or exp "Physical Therapy (Specialty)"/ or exp exercise therapy/ or kinesiotherapy.mp. or exp Exercise movement techniques/ or exercise movement technique\$.mp. or exercise technique.mp. or exercise therapy.mp. or breathing technique\$.mp. or exp respiratory therapy/ or pulmonary rehabilitation.mp. or breathing exercise\$.mp. or exp breathing exercises/ or physiotherapy.mp. or physiotherap\$.mp. or fan.mp. or exp complementary therapies/ or Complementary therap\$.mp. or complementary medicin\$.mp. or Alternative medicin\$.mp. or Alternative therap\$.mp. or yoga.mp. or meditation.mp. or acupuncture.mp. or acupressure.mp. or massage.mp. or exp musculoskeletal manipulations/ or musculoskeletal manipulation\$.mp. or exp Mind-Body/ or mind.mp.) and body.mp.) or mind-body.mp. or exp relaxation therapy/ or relaxation therapy.mp. or Relaxation Techniques.mp. or reflexology.mp. or relaxation.mp. or hypnosis.mp. or exp nutrition/ or nutrition.mp. or exp self-care/ or self care.mp. or self-help.mp. or self help.mp. or self-care.mp. or self-management.mp. or self management.mp. or exp

Appendix 1 Search strategy

counselling/ or counsel#ing.mp. or exp psychotherapy/ or psychotherapy.mp. or Non-pharmacological intervention\$.mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]

10. exp antidepressive agents/ or antidepressive agent\$.mp. or antidepressant\$.mp.

11. (amesergide or amineptine or amitriptyline or amoxapine or benactyzine or brofaromine or bupropion or butriptyline or cianopramine or citalopram or clomipramine or clorgyline or clovoxamine or demexiptiline or desipramine or dibenzepin or dimetacrin\$ or dosulepin or dothiepin or doxepin or etoperidone or femoxetine or fezolamine or fluoxetine or flupenthixol or fluphenazine or fluvoxamine or ifoxetine or imipramine or iprindole or iproniazid or phosphate or isocarboxazid or levoprotiline or lofepramine or l-tryptophan or maprotiline or medifoxamide or melitracen or metapramine or mianserin or milnacipran or minaprine or mirtazepine or moclobemide or nefazodone or nialamide or nomifensine or nortriptyline or opipramo or oxaflozane or oxaprotiline or oxitriptan or paroxetine or phenelzine or pirlindole or propizepine or protriptyline or quinupramine or reboxetine or rolipram or rubidium or sertraline or setiptiline or sibutramine or sulpiride or teniloxazine or tianeptine or tofenacin or toloxatone or tranylecypromine or trazodone or trimipramine or tryptophan or venlafaxine or viloxazine or viqualine or zimeldine).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]

12. exp benzodiazepines/ or anxiolytic\$.mp. or benzodiazepine\$.mp. or adinazolam.mp. or alprazolam.mp. or bentazepam.mp. or bromazepam.mp. or brotizolam.mp. or chlordiazepoxide.mp. or cinolazepam.mp. or clobazam.mp. or clonazepam.mp. or clorazepate.mp. or clotiazepam.mp. or cloxazolam.mp. or delorazepam.mp. or demoxepam.mp. or desmethyldiazepam.mp. or diazepam.mp. or estazolam.mp. or etizolam.mp. or etozolam.mp. or fludiazepam.mp. or flunitrazepam.mp. or flurazepam.mp. or flutoprazepam.mp. or halazepam.mp. or haloxazolam.mp. or ketazolam.mp. or loprazolam.mp. or lorazepam.mp. or lormetazepam.mp. or medazepam.mp. or metaclazepam.mp. or mexazolam.mp. or midazolam.mp. or nimetazepam.mp. or nitrazepam.mp. or nordazepam.mp. or oxazepam.mp. or oxazolam.mp. or pinazepam.mp. or prazepam.mp. or quazepam.mp. or temazepam.mp. or tetrazepam.mp. or tofisopam.mp. or triazolam.mp. or abecarnil.mp. or alpha hydroxymidazolam.mp. or alpidem.mp. or bretazenil.mp. or camazepam.mp. or chlorazepam.mp. or dealkylflurazepam.mp. or eszopiclone.mp. or ethyl loflazepate.mp. or imidazenil.mp. or ketazolam.mp. or loflazeplate.mp. or norchlordiazepoxide.mp. or

Appendix 1 Search strategy

norclobazam.mp. or paglone.mp. or persumbran.mp. or phenazepam.mp. or
premazepam.mp. or suproclone.mp. or suriclone.mp. or tuclazepam.mp. or zaleplon.mp.
or zapizolam.mp. or zolazepam.mp. or zolpidem.mp. or zopiclone.mp. [mp=title, original
title, abstract, name of substance word, subject heading word, unique identifier]

13. exp Analgesics, Opioid/

14. (morphine or fentanyl or hydromorphone, or oxycodone, or pentazocine or methadone
or opioid or opiate or opioids or opiates or codeine or dextromoramide or OTFC or
diamorphine or dihydrocodeine or dextropropoxyphene or meptazinol or sufentanil or
alfentanil or remifentanyl or nalbuphine or meptazinol or dipipanone or pethidine or
tramadol or buprenorphine).mp. [mp=title, original title, abstract, name of substance
word, subject heading word, unique identifier]

15. or/8-14

16. 7 and 15

17. Lung Diseases, Interstitial/dt, nu, rh, su, th, pc, dh, px or idiopathic interstitial
pneumonias/dt, nu, rh, su, th, pc, dh, px or idiopathic pulmonary fibrosis/dt, nu, rh, su, th,
pc, dh, px or pulmonary fibrosis/dt, nu, rh, su, th, pc, dh, px

18. 16 or 17

19. exp Evaluation Studies as Topic/

20. evaluation.mp.

21. 19 or 20

22. 18 and 21

Economic

1. exp idiopathic interstitial pneumonias/ or exp pulmonary fibrosis/

2. ((fibrotic NSIP or fibrotic lung disease or fibrotic non-specific interstitial pneumonia or
fibrotic non specific interstitial pneumonia or pulmonary fibrosis or IPF or cryptogenic
fibrosing alveolitis or interstitial pneumonia or UIP or IIP) not cystic fibrosis).mp. [mp=title,
original title, abstract, name of substance word, subject heading word, unique identifier]

3. 1 or 2

4. animal/

5. human/

6. 4 not (4 and 5)

7. 3 not 6

Appendix 1 Search strategy

8. Economics/ or "costs and cost analysis"/ or cost allocation/ or cost-benefit analysis/ or cost control/ or cost savings/ or cost of illness/ or cost sharing/ or "deductibles and coinsurance"/ or medical savings accounts/ or health care costs/ or direct service costs/ or drug costs/ or employer health costs/ or hospital costs/ or health expenditures/ or capital expenditures/ or value of life/ or exp economics, hospital/ or exp economics, medical/ or economics, nursing/ or economics, pharmaceutical/ or exp "fees and charges"/ or exp budgets/ or (low cost).mp. or (high adj cost).mp. or (health?care cost\$).mp. or (fiscal or funding or financial or finance).tw. or (cost estimate\$).mp. or (cost variable).mp. or (unit cost\$).mp. or (economic\$ or pharmacoeconomic\$ or price\$ or pricing).tw.

9. 7 and 8

Data extraction

One author (SB) screened all titles and abstracts. When multiple reports of a study were identified, they were treated as a single study and reference made to the full text if available. A Project Advisory Group and other experts in the field were asked to check the list to identify any known missing studies. A selection of papers were piloted using a data extraction sheet by applying the inclusion criteria to a sample of papers in order to check that they could be reliably interpreted and that they classified the studies appropriately. A data extraction sheet was completed for each paper passing the inclusion/exclusion stage. 2 authors (SB and JRR) extracted the data from all the full papers identified by SB except for the non-English papers for which data was extracted by SB in conjunction with translators. Disagreements for all papers were resolved by iteration and consensus. Data collected included study design, subject characteristics and study results as they pertained to the prespecified endpoints. Data for primary endpoints as stated by the authors has been extracted and presented.

Author and year of publication	Methods including design of study and	Quality (percentage of withdrawals, number used in analysis)	JADAD score	Primary objective Secondary objective	Participants Number Diagnosis and how diagnosed (with ref)	Intervention Control	Results	Notes including conclusions
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King 2009[1]	Randomised double blind, placebo controlled, multi-centre trial	N=826 enrolled, N=132 died (N=93 in IFN group, N=39 in placebo group)	5	Primary: To assess whether IFN gamma 1b SC improves survival in IPF patients. Secondary: To assess effect on symptoms, QOL and disease progression	ATS/ERS[2, 3] guidelines used- N=456 N=305 (55%) IFN, N=151 (55%) placebo biopsy confirmed	IFN gamma 1b SC 200mcg three times a week- half the dose for first 2 weeks and then full dose	No significant difference between IFN and placebo in effect on 6MWD, dyspnoea or quality of life.	Early termination of the trial occurred as secondary interim analysis did not show any improvement in survival. QOL, 6MWD and dyspnoea were secondary outcomes
Antoniou 2006[4]	Randomised, open label multicentre trial	Run in total N=68, N=50 underwent randomisation, N=12 died during study, N=21 completing study, N=50 included in analysis (ITT)	3	Primary: To assess the clinical effect of IFN gamma 1b and colchicine at 6,12 and 24 months of therapy Secondary: To assess adverse events	N=50 Histologically proven IPF (N=42 UIP on surgical biopsy) or fulfilled ATS/ERS criteria[3]	IFN gamma 1b SC 200mcg three times a week or colchicine 1mg/day orally in combination with low dose prednisolone	No significant difference in dyspnoea assessed by MRC scale, nor cough at each time-point. SGRQ QOL symptoms were significantly better after 12 months of treatment in interferon group- change in scores from baseline IFN -13.2 (-21.4, 5.0) mean (95% CI) and colchicine 7.5 (-4.5, 19.5) p=0.01	Improvement in SGRQ QOL symptoms with interferon gamma-1b compared to colchicine but not supported by other outcome measures, no power calculation undertaken for sample size
Strieter 2004[5]	Randomised double-blinded placebo controlled, multi-centre trial	N=32 enrolled, N=17 IFN group- N=17 completed. N=15 placebo group, N=1 discontinued N=1 died, N=13 completed. N=32 included in analysis	3	Primary: To assess the effects of IFN gamma 1b on biological markers of fibrosis in IPF. Secondary: To explore the effect on clinical measures such as dyspnoea, oxygen use and 6MWD	N=32 IPF- diagnosed using HRCT and tissue confirmation on all. ATS/ERS diagnostic criteria.	IFN gamma 1b SC 100mcg for first 2 weeks then 200mcg 3 times/week for 6 months, matched placebo	No significant difference in dyspnoea or 6MWD between intervention and control group	No significant difference in dyspnoea or 6MWD seen between intervention and placebo group

Author and year of publication	Methods including design of study and	Quality (percentage of withdrawals, number used in analysis)	JADAD score	Primary objective Secondary objective	Participants Number Diagnosis and how diagnosed (with ref)	Intervention Control	Results	Notes including conclusions
Zisman 2010[6]	Randomised double blind placebo controlled trial (multicentre) with open label following- data from open label presented separately below	N=180 randomised, N=89 sildenafil, N=79 completed sildenafil group, N=180 used in analysis	5	Primary: To demonstrate improved 6MWD in subjects with advanced IPF treated for 12 weeks with sildenafil compared to placebo. Secondary: To demonstrate improved dyspnoea and quality of life in patients with advanced IPF treated for 12 weeks with sildenafil compared to placebo	IPF ATS and ERS guidelines[3]	Oral sildenafil 20mg TDS or placebo	No significant improvement in 6MWD compared to placebo. Scores remained stable in the sildenafil group but worsened in placebo group on the SOB questionnaire (estimated difference, -6.58 p=0.006) and total score on St George's respiratory questionnaire (estimated difference, -4.08;p=0.01). SF36 there was no between group differences in the aggregate physical or mental sub scores however the general health sub score was better preserved in sildenafil group than placebo (absolute difference, 2.86;p=0.008). No significant difference in Borg Dyspnoea Index or EQ-5D scores.	No benefit of sildenafil compared to placebo for primary outcome of improving 6MWD. Improved dyspnoea and QOL in sildenafil group.
Zisman 2010[6]	Open label study following RCT to compare two arms receiving sildenafil. One arm has previously received sildenafil in the RCT, one has received placebo.	N=161, N=78 previously received sildenafil in RCT, N=83 previously received placebo in RCT	N/A	As primary study. In addition, second study used to estimate the 24 week safety and efficacy profile of sildenafil therapy.	As above	Oral sildenafil 20mg TDS	Among patients who were initially assigned to the placebo group but who received sildenafil during period 2, the 6MWD did not change significantly in the open label phase. There was also no significant change in the score on the SOB questionnaire, the activity score on SGRQ and the SF-36 general health and vitality scores.	No significant difference in 6MWD, dyspnoea or QOL scores between RCT and open label.

Author and year of publication	Methods including design of study and	Quality (percentage of withdrawals, number used in analysis)	JADAD score	Primary objective Secondary objective	Participants Number Diagnosis and how diagnosed (with ref)	Intervention Control	Results	Notes including conclusions
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Jackson 2010[7]	Randomised double blind placebo controlled single centre trial	N=29 included, N=14 sildenafil, N=15 placebo, N=3 withdrawn sildenafil, N=1 withdrawn placebo, N=26 included in analysis	5	Primary: To examine the effects of sildenafil on exercise tolerance. To compare changes from baseline in pre and post exercise dyspnoea	ATS and ERS clinical diagnostic criteria with exception of bronchoscopy[3] >30% had lung biopsies confirming UIP	Sildenafil citrate titrated: 20mg OD for 3 days, 20mg BD 3 days, 20mg TDS or placebo	No significant difference between placebo and sildenafil groups regarding 6MWD. No difference in secondary endpoint of dyspnoea at rest and after each 6MWT as measured by Borg scale.	Sildenafil did not significantly increase 6MWD or decrease the Borg dyspnoea index at rest or after 6MWT.
Collard 2007[8]	Quasi-experimental Open label study with no control	N=14 enrolled, N=0 died, N=11 completed study and included in analysis	N/A	Primary: To assess whether treatment with sildenafil would improve 6MWD in patients with IPF and PAH Secondary: To assess clinically meaningful response to sildenafil (defined as a >20% improvement in 6MWD and incidence of adverse events)	N=14 IPF ATS/ERS guidelines[2], N=6 biopsy proven	Sildenafil 20-50 mg TDS	Mean improvement in 6MWD was 49.0m (90% CI, 17.5, 84.0m). 57% of patients classified as responders.	Significant improvement in 6MWD in patients with IPF and PAH but numbers small. Not clear why a 90% CI was used
Holland 2008[9]	Randomised single blinded 2 site trial	N=57 randomised, N=34 IPF patients. N=20 intervention group, N=14 placebo. ITT	3	Primary: To assess functional exercise capacity before and after intervention using 6MWT Secondary: To	N=34 had diagnosis of IPF including 12 with biopsy confirmed UIP and remainder had typical findings of	Twice weekly exercise programme-completed programme if attended 12/16 sessions, control	Proportion of improved participants were similar in the subgroup of patients with IPF (73% in intervention group, 20% in control group). Mean difference [95%CI] in 6MWD of 16.12 [-13.32, 45.56]. No positive effect on MRC score but CRDQ scores improved in all domains (please see main paper)	Study powered to detect changes in 6MWD and all domains in CRDQ. Non-sustained improvement in 6MWD.

Appendix 2 Included studies

Author and year of publication	Methods including design of study and	Quality (percentage of withdrawals, number used in analysis)	JADAD score	Primary objective Secondary objective	Participants Number Diagnosis and how diagnosed (with ref)	Intervention Control	Results	Notes including conclusions
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		analysis used, missing data replaced with last observation carried forward		evaluate the safety of a standard exercise programme in ILD, to evaluate the effects of exercise training on exercise capacity, dyspnoea and QOL and whether there is a difference in response to exercise training in IPF compared to other ILDs	UIP on HRCT	group did not receive supervised exercise programme but were contacted once a week by telephone to provide support and general health advice		Improvements shown in exercise group for two dyspnoea scores and all of CRDQ QOL score.
Nishiyama 2008[10]	Randomised open label controlled trial	N=30, N=15 intervention, N=15 control. N=2 withdrew from intervention group	3	To assess the effects of pulmonary rehabilitation programme compared to usual care on pulmonary function, functional exercise capacity and health related quality of life	N=30 IPF diagnosed using ATS/ERS 2002 criteria[3] Unclear how many biopsy confirmed	10 week exercise programme with education lectures or control of usual care	After the programme, 6MWD and the total SGRQ score the mean difference [95%CI] for SGRQ total score of -6.1 [-11.7, -0.5] was found to be significant (p<0.05)	Improvement in 6MWD and health related quality of life seen
Ozalevli 2010 [11]	Quasi-experimental open label uncontrolled study	N=17, N=2 withdrew due to infectious disease, N=15 completed and	N/A	To investigate the effects of a home-based pulmonary rehabilitation	N=17 with IPF diagnosed using ATS/ERS consensus statement[2]	Home based pulmonary rehabilitation program for 12 weeks.	There was an increase in the 6MWD from baseline 390.3m to 430.5m (not clear whether mean value) post intervention (p=0.04) There was a significant decrease in perceived dyspnoea	Improvement in dyspnoea, and increase in 6MWD and general health related quality of life

Author and year of publication	Methods including design of study and	Quality (percentage of withdrawals, number used in analysis)	JADAD score	Primary objective Secondary objective	Participants Number Diagnosis and how diagnosed (with ref)	Intervention Control	Results	Notes including conclusions
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		used in analysis		program on functional outcome parameters in IPF			baseline MRCs score 2.3 (1.2) (mean (SD)) and after pulmonary rehabilitation 1.4 (1.3) (p=0.003). There was a found an improvement in general health related quality of life scores on SF36 mean (SD) (general health pre 57.0 (-4.6) post 74.0 (-4.7) p=0.04, physical role pre 25.0 (1.7) post 68.3 (1.6) p=0.01, and emotional role pre 29.0 (1.3) post 65.0 (1.4) p=0.02)	scores
Rammaert 2009[12]	Quasi-experimental open label uncontrolled study	N=17, N=2 died, N=13 completed study. N=13 included in analysis	N/A	To assess the impact of a pulmonary rehabilitation program on exercise capacity, pulmonary function, dyspnoea and quality of life	N=17 IPF ATS/ERS criteria[2]	8 week home base pulmonary rehabilitation program- if O ₂ saturations less than 90% when baseline 6MWT carried out then O ₂ titrated	Improvement in quality of life VAS scales looking at impact of treatment on daily life(p=0.002), dyspnea (p=0.025), quality of sleep (0.035), physical capacity (0.028). SF36 physical limitation score decreased significantly post intervention (p=0.047) No details of other SF36 scores given. SGRQ/HADs no significant changes post intervention. Non-significant changes in Borg (median (range) pre 4 (2-8) and post 3 (2-9) p=0.78 and MRC scales (pre 1.5 (1-3) and post intervention 2 (1-3) p=0.18.	O ₂ given to all patients and titrated therefore may have interfered in assessing effect of intervention. Little effect on QOL and SOB validated measures. Some VAS scores showed improvement post intervention (not validated in this group)
Kozu 2011[13]	Quasi-experimental open label study	N=90 enrolled. N=45 IPF, N=45 COPD, N=4 died in IPF group, N=36, N=30 completed at 8 weeks and 6 months for IPF group respectively, N=40 and N=37 completed at 6 months for COPD group	N/A	Primary: To evaluate the effects of pulmonary rehabilitation on dyspnoea, exercise capacity and health status in IPF patients compared to COPD control group	ATS/ERS n=9 had biopsies	8 week outpatient program of pulmonary rehabilitation with 2 classes each week including exercise training, breathing retraining and education. Completed if attended 75% of the 16 supervised sessions.	Significant improvements in 6MWD and dyspnoea occurred in both groups at 8 weeks compared to baseline. Baseline 6MWD IPF group 323m (109) and at 8 weeks 340 (122) p<0.01, baseline 6MWD COPD group 325m (107) and 8 weeks 378m (99) p<0.01. However these benefits were maintained at the 6 month follow up for the COPD group but not for the IPF group: 6 month 6MWD IPF group 320m (106) (not significant- value not given) 6 month 6MWD COPD score 367m (95) p<0.01. Baseline MRC grade IPF 3.0 (0.8) and at 8 weeks 2.5 (1.1) p<0.01, baseline MRC grade COPD group 3.0 (0.8) and at 8 weeks 2.3 (0.9) p<0.01. 6 month MRC scores were not significant. No improvement in QOL scores in the IPF group but all domains with the exception of social function improved in	Significant improvements in dyspnoea and 6MWD at 8 weeks but this effect lost by 6 months. The magnitude of improvements in all outcomes was less in IPF group than in COPD group.

Author and year of publication	Methods including design of study and	Quality (percentage of withdrawals, number used in analysis)	JADAD score	Primary objective Secondary objective	Participants Number Diagnosis and how diagnosed (with ref)	Intervention Control	Results	Notes including conclusions
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							the COPD group. The magnitude of improvements in all outcomes was less in IPF group than in COPD group.	
Swigris 2011[14]	Quasi experimental open label multicentre pilot study	N=21 patients enrolled in IPF group, N=2 died, N=14 completed, N=14 used in analysis	N/A	Primary: to investigate if a 6 week rehabilitation program improves functional capacity, fatigue, anxiety, depression, sleep and quality of life in IPF patients	N=21 IPF ATS/ERS criteria, N=14 had surgical biopsy	Pulmonary rehabilitation-exercise and education component. 18 sessions over 6-8 weeks. During PR SpO2 monitored and oxygen titrated to ensure that saturations remain >89%	6MWD Follow up data available for 8 IPF patients. 6MWD improved a mean (SE) 61.6m (41) (p=0.01). There was no significant improvement difference between the IPF and COPD groups. There was a significant improvement in Fatigue with mean change from baseline (95% CI) -1.5 (-2.48, -0.52) p=0.01 (no data available for COPD group). However there were no significant improvements in anxiety, depression, sleep quality or quality of life.	Sample size small and high dropout rate, comparison group were 56 COPD in another study.
King 2008[15]	Randomised double blind multicentre controlled trial - BUILD 1 trial	N=158 enrolled, N=74 bosentan, N=84 placebo, last observation carried forward or imputation, N=109 completed study N=154 used in analysis	3	To assess the effects of bosentan on exercise capacity and time to progression in patients with IPF.	N=158 IPF ATS/ERS criteria.[2] 68% of treatment and 60% of placebo group biopsy proven.	62.5mg bosentan orally twice daily for 4 weeks titrated to 125mg twice daily thereafter or matching placebo for at least 12 months.	Dyspnoea at the end of 6MWD using Borg Dyspnoea Index was more pronounced in placebo group compared with bosentan group up to 12 month (median treatment effect, -0.5;p=0.071). From similar baseline BDI, worsening TDI was significantly smaller for patients treated with bosentan than for patients treated with placebo TDI -0.6 bosentan and -1.9 placebo (p=0.016) at 6 months but not at the primary endpoint of 12 months -1.7 and -2.6 respectively (p=0.292). 42.4% of bosentan treated patients had an improved SF-36 health transition score compared with 28.4% of placebo-relative risk of improvement in favour of bosentan of 1.49 (95% CI, 0.96-2.33;p=0.084). Changes in seven of the eight domains of SF-36 up to 12 months were in favour of bosentan treatment, with a significant treatment effect in favour of bosentan observed in the domain role emotional (p=0.032) Total SGRQ score at baseline in bosentan group (mean, 45.7 (18.1)) was similar to that in placebo group (mean (SD), 45.2 (19)). Up to 6 months, the total score in bosentan	Bosentan showed no benefit compared to placebo for 6MWD. Changes from baseline up to 12 months in dyspnoea and QOL were seen for bosentan. Separate subanalysis completed for patients who had undergone surgical lung biopsy which favoured and showed a more pronounced effect on QOL.

Author and year of publication	Methods including design of study and	Quality (percentage of withdrawals, number used in analysis)	JADAD score	Primary objective Secondary objective	Participants Number Diagnosis and how diagnosed (with ref)	Intervention Control	Results	Notes including conclusions
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							<p>group remained almost unchanged (mean (SD), 45.0 (21.3)) but worsened in placebo group (mean (SD), 47.8 (21.7)), representing a mean (SEM) treatment effect of -3.3 (2.6) (p=0.034). Mean treatment differences up to 12 months continued to favour bosentan but were smaller (data not provided).</p> <p>Subset analysis of surgical biopsy proven IPF treatment effects observed at 12 months in favour of Bosentan group in 3 domains of SF-36: "physical functioning" (p=0.041), "general health" (p=0.012), and "role emotional" (p=0.037). Up to 6 months, the mean total SGRQ score in the bosentan treated sub-group remained similar to baseline (mean (SD), 43.6 (18.2)) but worsened in the placebo-treated subgroup (mean (SD) , 49.2 (-21.3)) a mean (SEM) treatment effect of -7.3 (2.8) (p=0.010) in favour of bosentan. Up to 12 months the mean total SGRQ scores favoured treatment with bosentan (mean (SD), 46.1 (19.9)) versus placebo (mean (SD), 51.1 (23.7)) - a mean (SEM) treatment effect of -6.6 (3.0) (p=0.058).</p>	
Raghu 2010[16]	Second paper published from BUILD 1	As above	As above	To examine longitudinal changes in HRQOL and dyspnoea in IPF on patients on bosentan compared to placebo	As above	As above	<p>At 6 months, a change from baseline in SGRQ total score indicated improvement in bosentan patients; however, up to 12 months no differences were observed between treatment groups in any domain of SGRQ. SF-36 showed no difference at 6 months but at 12 months there was a change from baseline in role emotional domain of placebo-treated patients suggesting improvement in bosentan-treated patients. (data not given)</p> <p>SLB subset- In addition, treatment effects were observed at 12 months in the impact domain of the SGRQ (median treatment effect -7.0 p=0.03) and the physical functioning (MTE 9.3 p=0.04, general health (MTE=9.4 p=0.01) and role emotional domains of the SF-36 (MTE 0.0 p=0.04).</p> <p>At 6 months, the number of subjects with improved dyspnoea identified by TDI of greater than or equal to 1 was 18 (26.9%) in bosentan group and 10 (12.2%) in the</p>	As above

Author and year of publication	Methods including design of study and	Quality (percentage of withdrawals, number used in analysis)	JADAD score	Primary objective Secondary objective	Participants Number Diagnosis and how diagnosed (with ref)	Intervention Control	Results	Notes including conclusions
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							placebo group, corresponding to a relative risk of 2.2 (95% CI 1.1-4.5). This effect is not apparent up to 12 months (relative risk 1.0;95% CI 0.5-2.0). In SLB subset, upto 12 months, the Borg score was unchanged in the bosentan group and had changed from 0.0 (95% CI 0.0-0.0) to 1.0 (0.0-1.0) in the placebo group, a treatment effect of bosentan of 1.3 (95% CI 0.0-2.9;p=0.03). At 6 months, the number of subjects in SLB subset with improved dyspnoea identified by a TDI of greater than or equal to 1 was 12 (25.0%) in the bosentan group and 4 (8.2%) in placebo group, corresponding to a relative risk of 3.1 (95% CI 1.1-8.8). This effect was not apparent upto 12 months (relative risk 0.9;95% CI 0.4-2.1).	
King 2011[17]	Randomised double blind placebo controlled trial with parallel group	N=616 enrolled, N=407 bosentan, N=209 placebo, N=17 (N=11 bosentan) died during study, N=615 included in analysis-ITT and N=1 not treated	5	Primary: To demonstrate the effect of bosentan on delaying IPF progression/survival Secondary: To assess the effect of on HRQOL, dyspnoea and pulmonary function	IPF by ATS/ERS[2] with all participants having confirmed surgical biopsy.	Bosentan 62.5mg BD for 4 weeks and then titrated to 125mg BD if weight equal or greater than 40kg or matched placebo until 202 primary endpoints acheived	No treatment effects were observed on health related quality of life or dyspnoea.	No benefit of bosentan shown on QOL or symptoms compared to placebo.
Noble 2011[18] CAPACITY 004	Double blind randomised placebo controlled trial-multi-centre	N=435 enrolled, N=18 deaths, N=348 included in efficacy analysis. The group assigned to pirfenidone 1197mg/day was summarised descriptively.	5	Primary: To assess whether pirfenidone reduces deterioration in lung function in patients with IPF Secondary: include categorical FVC,	Patients younger than 50 y and those not meeting protocol criteria for definite IPF by HRCT were required to have lung biopsy showing UIP	Patients assigned in a 2:1:2 ratio to pirfenidone 2403mg/day, pirfenidone 1197mg/day or placebo for a minimum of 72 weeks	Mean change in USCD not significant. Pirfenidone did not significantly reduced decline in 6MWD- Absolute difference (95% CI) 16.4 m (-10.9 to 43.7). No Qol data	No change in dyspnoea or 6MWD. No efficacy data for lower dose of pirfenidone.

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				progression free survival, dyspnoea and 6MWD	surgical biopsy pirfenidone 1197mg/day 32 (37%), pirfenidone 2403mg/day 86 (49%), placebo 85 (49%)			
Noble 2011[18] CAPACITY 006	Double blind randomised placebo controlled trial- multi-centre	N=344 enrolled, N=12 died, N=344 included in analysis	5	Primary: To assess whether pirfenidone reduces deterioration in lung function in patients with IPF Secondary: include categorical FVC, progression free survival, dyspnea and 6MWD	Patients younger than 50y and those not meeting protocol criteria for definite IPF by HRCT were required to have lung biopsy showing UIP surgical biopsy pirfenidone 94 (55%), placebo 94 (54%)	Patients assigned in a 1:1 ratio to pirfenidone 2403mg/day or placebo for a minimum of 72 weeks	Mean change in USCD not significant. Pirfenidone significantly reduced decline in 6MWD- Absolute difference (95% CI) 31.8m (3.2 to 60.4). No QoL data	No change in dyspnoea but improvement in 6MWD. Pooled data from study 004 and 006: absolute difference (95% CI) 24.0 m(4.3 to 43.7)
Tomioka 2005[19]	Open, non-blinded RCT (pilot study)	N=30 enrolled, N=15 both arms, N=10 completing NAC arm, N=12 completing bromhexine arm, N=22 included in analysis	3	Primary: To assess the effectiveness of NAC in altering the decline in lung function, 6MWT and HRCT progression. Secondary: Effects on serum KL-6 and HRQOL	N=4 diagnosis based on presence of UIP by surgical biopsy, N=26 based on ATS and ERS 2000 consensus[2]	NAC 325mg/day inhaled, control- bromhexine hydrochloride 4mg/day inhaled for 12 months	No significant differences observed for 6MWD or HRQOL	No significant treatment effect observed for 6MWD or HRQOL. Steroids were started in 3 patients due to disease progression (control N=2 and NAC N=1)
Demedts 2005[20]	Double blind randomised placebo	N=182 enrolled, N=15 died, N=108	4	Primary: To assess the effect of NAC on	Mandatory biopsy in patients <50 years of age.	NAC- 600mg TDS or matched placebo, Both	No significant difference in dyspnoea or QOL	No significant differences in dyspnoea or QOL

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	controlled trial- multi-centre	completed, N=155 included in analysis		pulmonary function. Secondary: To assess the effect on dyspnoea, quality of life and disease progression, SE profile of intervention	ATS/ERS diagnosis criteria. [2, 3]	groups received prednisolone and azathioprine (2mg/kg/day)		
Varney 2008[21]	Randomised double blind placebo controlled pilot study	N=20, N=10 active treatment, N=10 placebo, no withdrawals	5	To assess the benefit of oral co-trimoxazole alone or in combination with oral prednisolone on exercise capacity, lung function and quality of life	N=20 with progressive fibrotic lung disease (IIP) with physical examination, HRCT scan and pulmonary function tests compatible with advanced fibrotic lung disease (UIP or NSIP or mixed +/-histological diagnosis). N=4 co-trimoxazole and N=3 placebo HRCT pattern of UIP, N=5 co-trimoxazole, N=4 placebo HRCT pattern UIP/fibrotic NSIP, N=1 co-trimoxazole and N=3 unclassifiable	Co-trimoxazole or identical placebo with dosage according to body weight (upto 70kg received 960mg BD, greater than 70 kg received 3 times 480mg BD). Folic acid was given 3 times a week and ranitidine 150mg BD was supplied but optional) Total duration of treatment 5months- 3 months active/placebo treatment, followed by 6 weeks pulmonary rehabilitation with decode 2 weeks post rehabilitation	MRC dyspnoea score showed improvement with a median score (95% CI) of 3(2.0,4.0) pretreatment 2 (1.0-3.0) post-treatment at 3 months for the active group (p=0.05) which was maintained at 12 months. SGHRQ showed significant reduction in symptom scores (pre-treatment 64.2 (21.7) mean (SD) and at 12 months (44.5 (20.7) (p=0.05)). Borg breathlessness score and VAS were significantly improved (data not presented in paper). Improvement in cough within 4 weeks of treatment (p=0.002) data not presented in paper. Treatment effect data analysed at 12 months.	Co-trimoxazole may be helpful in improving SOB and cough. QOL and Prednisolone was taken by 55% of patients- difficult to assess contribution of this. No power calculation and small numbers.

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					HRCT fibrotic (mixed)			
Raghu 2008[22]	Randomised prospective double blind placebo controlled multicentre phase II trial	N=88, N=46 randomised to Etanercept with N=34 completing. N=41 randomised to placebo with N=31 completing, N=87 included in analysis	3	Primary: To investigate the efficacy and safety of etanercept as therapy for IPF Secondary: to assess its effects on quality of life and mortality	N=88 IPF as diagnosed by ATS/ERS consensus statement[2]	Etanercept SC 25mg twice weekly for 48 weeks or placebo	No significant improvements in QOL, dyspnoea or 6MWD.	No improvement in QOL, dyspnoea or 6MWD.
Krowka 2007[23]	Randomised double blind placebo controlled multi-centre trial	N=51 enrolled N=26 Iloprost N=25 placebo N=6 dropped out of iloprost group and N= 9 out of Placebo group	3	Primary: To assess safety of inhaled iloprost Secondary: to assess efficacy and effect on exercise, symptoms, exercise induced O ₂ sats and clinical status	N=51 IPF patients- no details on how diagnosed	Inhaled Iloprost (2.5mcg or 5mcg per dose:6-9 doses/day) for 12 weeks or matched placebo	No significant differences between intervention and placebo from baseline in 6MWD (-31m vs 9.8m for iloprost and placebo respectively), NYHA class (16% vs 13% improved) or Borg Dyspnoea Score.	No evidence of clinical benefit. Poster therefore limited information- unclear how many patients included in analysis. Patients randomised to Iloprost were less severely impaired than those randomised to placebo. Secondary efficacy endpoints were not met.
Lindell 2010[24]	Randomised controlled trial with control	N=42 enrolled but included patients and	2	Primary: to assess the impact of a disease	14% of intervention and 43% of control	Intervention- program delivered using format of	There was no statistically significant difference in end mean (SD) scores in the Shortness of Breath Questionnaire for intervention 49.51 (22.64) or control 49.88 (22.64) p=0.972,	Quantitative outcome measures showed greater anxiety in

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	group, concurrent mixed method design.	carers. Only N=21 patients, N=1 patient died during study, N=19 patients completing.		management program on symptom management and health related quality of life Secondary: to assess the impact on carers	group had biopsy	support group with 6 weekly group sessions attended by patients and carers. Control- usual care consisted of being seen by members of clinical care team at interviews of 3-6 months	Perceived Stress Scale for intervention 19.32 (3.64) and control 18.20 (3.65) $p=0.531$ and Beck Depression Index for intervention 9.71 (4.34) and control 9.44 (4.35) $p=0.894$. The mean end Beck Anxiety Index scores approached statistical significance intervention 15.13 (6.92) and control 8.56 (6.95) $p=0.077$ reflecting increased anxiety in the intervention group. Intervention had negative impact on patients (experimental group rated their HRQOL less positively after intervention $p=0.038$ and tended to report more anxiety $p=0.077$ than controls) . This is contradictory to what found in qualitative work which consisted of 19 interviews of experimental group participants who didn't feel isolated and felt the intervention had enabled them to put the disease into perspective, gave comfort and provided an improved mental picture.	patients receiving the intervention and a negative impact on some quality of life scores. Contradictory to what was found in qualitative work.
Hope-Gill 2003[25]	Open label-no control	N=6 No withdrawals	N/A	To assess the effect of prednisolone on capsaicin induced cough	N=6 IPF diagnosed using ATS/ERS 2000 criteria[3] with VAS cough score greater than 5	Oral prednisolone 40-60mg/day+ omeprazole 20mg/day for 4 weeks	Significant reduction in cough reflex sensitivity to capsaicin ($p<0.05$). Reduction in mean VAS score from 7.2+/-0.8 to 2.2+/-2.5 ($p<0.05$) at 4 weeks. Only 5/6 patients data reported as one patient unable to reliably indicate cough severity using VAS	Subset of main study- Not clear whether inclusion /exclusion criteria listed in main study apply to these 6 patients- no age/male, female data. Reduction in artificially induced cough. Intervention included omeprazole to be given for 1/12 before start of study which may have improved GORD related cough.

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Turner-Warwick[26]	Retrospective review of case notes	N=220 but only N=143 received steroids, outcome data available for N=127	N/A	To distinguish factors influencing an early response to treatment. To assess influence of steroid treatment on survival	N=143 CFA-diagnosed by using Turner Warwick criteria[27]	Prednisolone various doses	After 4-6 weeks of treatment 55 (43%) classified as non-responders and 72 (57%) as responders from dyspnoea.	Majority classed as dyspnoea responders. N=143 given steroids but outcome data only available on N=127- difficult to elicit information from paper.
Fiorucci 2008[28]	Open label single centre, 3 arm study	N=30, N=11 group 1 of which N=4 died, N=9 group 2 of which N=4 died, N=10 group 3 of which N=3 died. N=30 included in analysis	N/A	To evaluate the role of colchicine, cyclophosphamide and prednisolone on efficacy, tolerability and impact on survival	N=30 IPF on ATS ERS[2, 3] criteria, N=8 had VATS biopsy, N=25 had transbronchial biopsy	Group 1: Prednisolone alone- 1mg/kg/day for 4/52 then 0.5mg/kg/day for 2 months followed by gradual reduction to 20mg/day. Group 2: Prednisolone 0.5mg/kg/day for 1 month, 0.25mg/kg/day for 2 months following reduction + oral cyclophosphamide 100mg/day. Group3: Prednisolone 0.5mg/kg/day then reduced+ colchicine1mg/day	Significant improvement in dyspnoea in colchicine and prednisolone group. Baseline dyspnoea 8.4 +/-2.5 and at 18 months 6.3 +/-2.2 P=0.001. Two patients of group 1 (18%), one patient of group 2 (11%) and eight patients of group 3 (80%) showed a decrease of dyspnoea (p=0.001). Analysis of score variations from baseline to follow up showed a significant difference in group 3 (average -2.1+/-1.3, 95% confidence interval -5.4 and 0.7) as compared with group 1 (average 3.1 +/-1.5, 95% confidence interval -0.2 and 6.5) and group2 (average 4.1 +/-1.9, 95% confidence interval -0.3 and 8.5) p=0.03	Single centre study and small numbers but some improvement in dyspnoea in colchicine and prednisolone treated group compared to other groups

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Hicks 2007[29]	Retrospective case note study	N=70 N=41 already using O ₂ prior and performed baseline test with O ₂ , N=29 not using O ₂ prior and performed baseline without O ₂	N/A	To assess the benefits of ambulatory oxygen on 6MWD and dyspnoea in patients with IPF comparing patients who were on O ₂ prestudy with those who were not	N=70 IPF diagnosis using ATS/ERS criteria[3]	Ambulatory oxygen- may be increased during test (at 2L increments) – all patients required to have PaO ₂ levels >8kPa to commence test	Patients not on O ₂ pretest managed to walk a statistically significant 81.2m (mean) p<0.01 further using optimal O ₂ therapy. Patients already on O ₂ walked an extra 16.9m (mean) p=0.02. Borg scores at test end were not significantly different using optimum O ₂ compared to baseline tests	IPF patients receive benefit from ambulatory oxygen in terms of distance walked. This is more marked in those not on O ₂ pre-therapy. Retrospective case note analysis and poster therefore limited information.
Visca 2011[30]	Retrospective case note study	N=52 in total study, N=34 IPF/NSIP patients	N/A	Primary: To assess the effect of ambulatory O ₂ on 6MWD for ILD patients. Secondary: To assess the effect on dyspnoea	N=34 IPF/NSIP, N=8 ILD associated with connective tissue disease. N=10 fibrotic granulomatous disease using ATS/ERS criteria but unclear how many biopsy proven	Ambulatory O ₂ - dose decided on individual oxygen requirements based on desaturation on baseline test, patients BMI, gender and whether cylinder to be carried by patient or others.	In subgroup of IPF and NSIP patients ambulatory O ₂ significantly improved 6MWD from baseline 272.3m +/-19.8 mean +/- SE to 304.7 +/-17.8 at endpoint (p=0.0001) and Borg score recovery time from 167.1 +/-28.2 sec at baseline to 120.7 +/-15.5 sec on oxygen (additional or increased) (p=0.008). Dyspnoea as measured by Borg scale also improved with O ₂ 4.25(3-5) (median and 95% CI) at baseline compared to 3.25 +/- (2.5-4) on O ₂ (<0.00001).	Improved 6MWD, dyspnoea and Borg recovery time in patients using ambulatory oxygen. Retrospective case note analysis with no control.
Allen 2005[31]	Quasi-experimental, open label study	N=11	N/A	Primary: To assess effectiveness of diamorphine on breathlessness Secondary: To assess side effects	Characteristic changes on CXR, N=6 had previous CT supporting diagnosis and 8 had restrictive pattern on spirometry	Diamorphine sc 2.5mg (< or 60kg), 5mg (>60kg)	No adverse effects on vital signs and oxygen saturation but substantial fall in dyspnoea analogue score from mean baseline (SD) 83(13) to 36 (11) at 15min and 36 (12) at 30min p<0.001 after administration of diamorphine. In addition there was a fall in observed anxiety (no details given).	Improvement in SOB with diamorphine without significant adverse effects. No details of objective improvements in anxiety and no subjective measurements. Poor diagnostic criteria for IPF.

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Hanania 1993[32]	Quasi-experimental open label uncontrolled study	N=10, N=3 died, N=10 included in analysis	N/A	To assess the effects of D-pencillamine	N=10 IPF- no criteria given	D-pencillamine- initially dose of 250mg/day which is then increased by increments of 250mg/week up to a maximum of 4000mg/day	N=5 improved by at least one full grade of NYHA criteria. N=1 had no change, N=3 deteriorated	50% showed improvement but numbers small and no diagnostic criteria given- limited data as abstract only
Lutherer 2010 [33]	Quasi-experimental Open label single arm study	N=20, N=3 died during study, N=12 completing, N=12 included in overall analysis but only N=6 completed Leicester Cough Questionnaire (LCQ)	N/A	Primary: To assess the efficacy of oral interferon alpha on the progression of IPF. Secondary: to assess the effect on symptoms	N=20 IPF diagnosed using ATS/ERS consensus statement , N=3 had lung biopsies unclear which patients, N=20 had HRCT	Interferon alpha lozenge, 150IU TDS	Five of the six subjects with chronic cough on entry reported an overall improvement within two to three weeks after starting treatment. Three reported decreases in the frequency, the duration, and the intensity of their cough, and two reported decreases in at least one of these categories. Night-time coughing was eliminated in four subjects. Five of six subjects with a chronic cough who completed the Leicester Cough Questionnaire had an improvement in their total score.	Improvement in cough but numbers were small
Agusti 1993[34]	Quasi-experimental Open label- no control	N=10 No withdrawals	N/A	Evaluate efficacy of ribavarin in patients with CFA	N=10 CFA-diagnosis by lung biopsy in 2 patients. In remaining by Turner-Warwick criteria. [35]	6g of ribavarin dissolved in water delivered via aerosol generator delivered for seven hours daily for 14 days	No significant change in dyspnoea on a 5 point scale after treatment with aerosolized ribavirin baseline dyspnea 2.4 (1), 3 month 2.3 (1.1) and 12 month 2.7 (0.1). We have assumed these to be mean (SD) as not clear from paper.	No significant change in dyspnoea.
Horton 2008[36]	Quasi-experimental open label study with no control	N=11, N=11 completed and analysed but only N=6 data available for SGRQ and cough	N/A	Primary: To assess the effect of thalidomide on cough in IPF patients	N=IPF, no diagnostic criteria given	Thalidomide 100-400mg	10/11 experienced marked or complete resolution of cough. SGRQ data only available for N=6- showed significant decrease in score from baseline 4.9 (0.3) to 2.2 (1.6)(p=0.03 after 3 months). N=3 who stopped taking thalidomide all experienced return of cough within 2 weeks but with reinstitution, all three patients again had resolution of cough.	Improvement of cough with thalidomide but small numbers
Undurraga	Quasi-	N=17, N=7	N/A	Primary: To	N=17 IPF as	Colchicine 0.5-	Improvement in dyspnoea in 10/17 patients of an average	Some improvement in

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1998[37]	experimental open label, no control	completing study, N=17 included in analysis		evaluate the clinical, radiological and physiological effect of colchicine Secondary: To assess possible side effects of treatment	diagnosed using Turner Warwick criteria. [27] N=4 had biopsies of which N=1 was transbronchial	1mg/day, N=14 had 1mg/day, N=3 had 0.5mg/day. N=7 completing trial had treatment for a mean of 21 months	of 1.7 units (significance unclear). 7 patients did not notice any change.	breathlessness but unclear whether this is significant. Likely to be mixed group of patients.
Mishra 2011[38]	Quasi-experimental Open label uncontrolled trial	N=6, N=5 completing, N=6 included in analysis	N/A	Primary: Effect of doxycycline on matrix metalloproteinase (MMPs) activity and clinical outcomes	N=6 IPF diagnosed using ATS/ERS. No biopsies done.	Doxycycline 100mg OD if weight less than 50kg, 200mg BD if greater	SGRQ improved significantly Mean (SD) Before 50.90 (8.38), after 18.40 (6.39) p<0.001 but no significant improvement in 6MWD	Improvement in QOL but numbers small.

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Study	Reason for exclusion
Abernethy 2010 ¹	Unable to separate PIF-ILD data
Abernethy 2003 ²	Unable to separate PIF-ILD data
Addrizzo-Harris 2002 ³	Unable to separate PIF-ILD data
Azuma 2005 ⁴	No extractable data
Behera 1998 ⁵	Subjective improvement, no outcome measurements used
Behr 1997 ⁶	Unable to separate PIF-ILD data. No outcome measures used.
Bhattacharyya 2009 ⁷	No appropriate outcome measures
Chapela 1986 ⁸	No extractable data
Dimadi 2003 ⁹	No appropriate outcome measures
Douglas 1998 ¹⁰	No extractable data
Fasciolo 1994 ¹¹	Unable to separate PIF-ILD data
Ferreira 2006 ¹²	Unable to separate PIF-ILD data
Ferreira 2009 ¹³	Unable to separate PIF-ILD data
Flaherty 2001 ¹⁴	Unable to separate out dyspnoea data
Glockl 2009 ¹⁵	No extractable data
Gomez 2007 ¹⁶	Incomplete study
Gross 1995 ¹⁷	Unable to separate PIF-ILD data
Gunella 1991 ¹⁸	Unable to separate PIF-ILD data
Janssen 2010 ¹⁹	No extractable data
Jastrzebski 2006 ²⁰	Unable to separate out PIF-ILD data
Johnson 1989 ²¹	Unable to extract dyspnoea data from paper
Kalra 2003 ²²	No appropriate outcome measures
Lanuza 2000 ²³	Unable to separate PIF-ILD data
Leung 1996 ²⁴	Unable to separate PIF-ILD data
Naji 2006 ²⁵	Unable to separate PIF-ILD data
Peters 1993 ²⁶	No appropriate outcome measures.
Raghu 2004 ²⁷	No extractable data
Rodrigue 2005 ²⁸	Unable to separate PIF-ILD data
Salhi 2010 ²⁹	Unable to separate PIF-ILD data
Scano 1981 ³⁰	Unable to separate PIF-ILD data
Selman 1998 ³¹	No extractable data
Sharifabad 2010 ³²	Unable to separate PIF-ILD data
Stack 1972 ³³	No appropriate outcome measures
Sturani 1988 ³⁴	No appropriate outcome measures
Swinburn 1991 ³⁵	Unable to separate PIF-ILD data
Taniguchi 2010 ³⁶	No extractable data
TenVergert 1998 ³⁷	Unable to separate PIF-ILD data
Webb 2000 ³⁸	Not clear that any IPF patients are included.
Young 1989 ³⁹	No appropriate outcome measures
Ziesche 1999 ⁴⁰	No appropriate outcome measures
Zisman 2000 ⁴¹	No extractable data

Appendix 3 Potentially relevant excluded studies

1. Abernethy AP, McDonald CF, Frith PA, Clark K, Herndon JE, 2nd, Marcello J, et al. Effect of palliative oxygen versus room air in relief of breathlessness in patients with refractory dyspnoea: a double-blind, randomised controlled trial. *Lancet* 2010;376(9743):784-93.
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Appendix 3 Potentially relevant excluded studies

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Appendix 3 Potentially relevant excluded studies

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Study	Outcome measure with original reference where given in paper
Antoniou 2006[1]	Medical Research Council (MRC) dyspnoea scale[2] Cough- Dry, productive, absent (no reference) St George's Respiratory Questionnaire (SGRQ) [3, 4]
King 2009[5]	University of California San Diego shortness of breath questionnaire (UCSD)[6] SGRQ[7]
Strieter 2004[8]	Modified MRC scale (no ref) Baseline Dyspnoea Index (BDI) and Transition (endpoint) dyspnoea index (TDI) (no ref) UCSD (no ref)
Jackson 2010[9]	Borg dyspnoea scale (modified 10 point)[10]
Zisman 2010[11]	UCSD [12] Borg dyspnoea index [13] SGRQ [14] SF-36 [14] EQ-5D [15]
Collard 2007[16]	Borg Dyspnoea Index (no ref)
Nishiyama 2008[17]	BDI [18] SGRQ [19]
Holland 2008[20]	MRC scale (modified)[2] SF-36[7] Chronic Respiratory Disease Questionnaire (CRDQ)[7]
Ozalevli 2010[21]	MRC scale [22] Borg dyspnoea Index (modified) [2] SF-36 (Turkish version) [23]
Rammaert 2009[24]	Baseline Dyspnoea Index [25] Borg Dyspnoea Index [26] MRC scale [27] SF-36 [28] SGRQ [29] Hospital Anxiety and Depression scale [30] 7 questions in Visual Analogue Scale looking at symptoms and quality of life
Kozu 2011[31]	MRC scale [32] BDI & TDI [18] SF-36 version 2 (Japanese version)[33]
Swigris 2011[34]	Fatigue Severity Scale[35] General Anxiety Disorder-7 scale[36] Patient Health Questionnaire-8 [37] Pittsburgh Sleep Quality Index [38] SF-36 [37]
King 2011[39]	Baseline Dyspnoea Index Transition Dyspnoea Index [18] SF-36[40] EQ5D[41]
King Jr 2008 (BUILD 1)[42] Raghu 2010 (2 nd paper BUILD 1)[43]	Borg Dyspnoea Index [26] Baseline Dyspnoea Index Transition Dyspnoea Index [18] SF-36[44] SGRQ[3]
Noble 2011[45]	UCSD[6]
Tomlioka 2005[46]	SF-36 (Japanese version) [33, 47]
Demedts 2005[48]	Dyspnoea Score[49] SGRQ [3]
Varney 2008[50]	MRC scale (no ref) SGRQ (no ref)
Raghu 2008[51]	Mahler dyspnoea scale (no ref) SF-36 (no ref) SGRQ[52]
Krowka 2007[53]	Borg Dyspnoea Index (no ref) NYHA class (no ref)
Lindell 2010[54]	UCSD[6] Beck Anxiety Inventory[55] Beck Depression Inventory-II[56] Perceived Stress Scale[57] SF-36[58]
Hope-Gill 2003[59]	Visual Analogue Scale for cough (no ref)
Turner-Warwick 1980[60]	4 step improvement in dyspnoea scale (no ref)
Fiorucci 2008[61]	20 point dyspnoea scale (as part of clinical radiologic physiologic-CRP scoring system) [49, 62]
Hicks 2007[63]	Borg dyspnoea index (no ref)
Visca 2011[64]	Borg dyspnoea index [26]
Allen 2005[65]	Visual Analogue Scale for dyspnoea (no ref)
Hanania 1993[66]	NYHA criteria (no ref)
Lutherer 2011[67]	Leicester Cough Questionnaire[68]
Agusti 1993[69]	5 point dyspnoea scale[70]
Horton 2008[71]	Question 2 on SGRQ (no ref) for assessment of cough
Undurraga 1998[72]	20 point dyspnoea scale (as part of clinical radiologic physiologic-CRP scoring system) [49]
Mishra 2011[73]	SGRQ (no ref)

Appendix 4 Outcome measures

1. Antoniou KM, Nicholson AG, Dimadi M, et al. Long-term clinical effects of interferon gamma-1b and colchicine in idiopathic pulmonary fibrosis. *European Respiratory Journal*. 2006 Sep;28(3):496-504.
2. Mahler DA, Wells CK. Evaluation of clinical methods for rating dyspnea. *Chest*. 1988 Mar;93(3):580-6.
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16. Collard HR, Anstrom KJ, Schwarz MI, et al. Sildenafil improves walk distance in idiopathic pulmonary fibrosis. *Chest*. 2007;131(3):897-900.
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19. Jones PW, Quirk FH, Baveystock CM, et al. A self-complete measure of health status for chronic airflow limitation. The St. George's Respiratory Questionnaire. *American Review of Respiratory Disease*. 1992 Jun;145(6):1321-7.
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Appendix 4 Outcome measures

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Appendix 4 Outcome measures

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1.6.2 Summary of systematic review

1.6.2.1 Main points from systematic review

- Paucity of evidence for any intervention to improve symptom control;
- Evidence for pulmonary rehabilitation and sildenafil in improving QoL;
- Only 4 RCTs with the primary outcome of symptom improvement or QoL;
- Primary focus of research in this area has been for radical interventions.

1.6.2.2 Implications from the review related to the study

There has been a focus on developing radical interventions (focussed on improving survival) in this group. In developing a palliative intervention (focussed on improving symptoms and QoL), I would need to focus on using appropriate primary outcomes related to symptom control and QoL.

In addition, the methodological quality of studies focusing on developing palliative interventions has been low. Where possible, robust study designs (such as RCT) should be used in evaluating a palliative intervention.

1.7 The palliative care needs of patients and informal caregivers with PIF-ILD

In this section, I will present the evidence for the palliative care needs of patients and informal caregivers. Alongside the previous section, this will form the *identifying the evidence base* part of the **Development** stage of the MRC guidance. I will show that there is limited research related to palliative care needs of this group and that there are unmet patient and informal caregiver concerns and information needs. I will then present a retrospective review of medical notes/audit conducted as background work to gain some preliminary understanding of the palliative care needs of these patients which will form the background for the *identifying or developing theory* part of the **Development** stage.

1.7.1 Current evidence base

No primary research has been conducted to assess the palliative care needs of patients and informal caregivers with PIF-ILD. However, there have been studies which have focused on supportive and general care needs which are relevant to this research. Schoenheit et al (36) undertook single in-depth interviews with 45 IPF patients from five European countries. The authors asked participants to select images that expressed their feelings and asked them to recall what was said in a particular situation. IPF was found to have a substantial impact on daily life in terms of reduced independence, difficulty in continuing relationships and struggling financially through being unable to work. The study also collated details of symptoms and revealed that dyspnoea was experienced by 68% of participants, 59% reported a cough and 28% reported fatigue. In addition, there have been two qualitative studies (37, 38) which have focussed on identifying factors which may affect QoL in the development of/evaluation of QoL tools. A Dutch study conducted focus groups of 10 IPF patients to identify the aspects of QoL or health status relevant to the patients in comparing two QoL measures.(37) No formal qualitative analysis was performed but the investigators reported findings from the focus groups. Swigris et al conducted a study of 20 IPF patients using focus groups and individual in-depth interviews to assess patients' perspectives on how IPF affected the quality of their lives.(38) The aim of this study was to identify domains which could then be used to aid development of a QoL instrument. Both of these studies suggested IPF patients experience an adverse effect on physical health,

general health, energy levels, respiratory symptoms and level of independence. Swigris et al (38) analysed patients' perspectives and organised them into a conceptual framework consisting of 12 domains. A diagrammatic representation of the Swigris paper is found in Figure 1-5 Page 80.

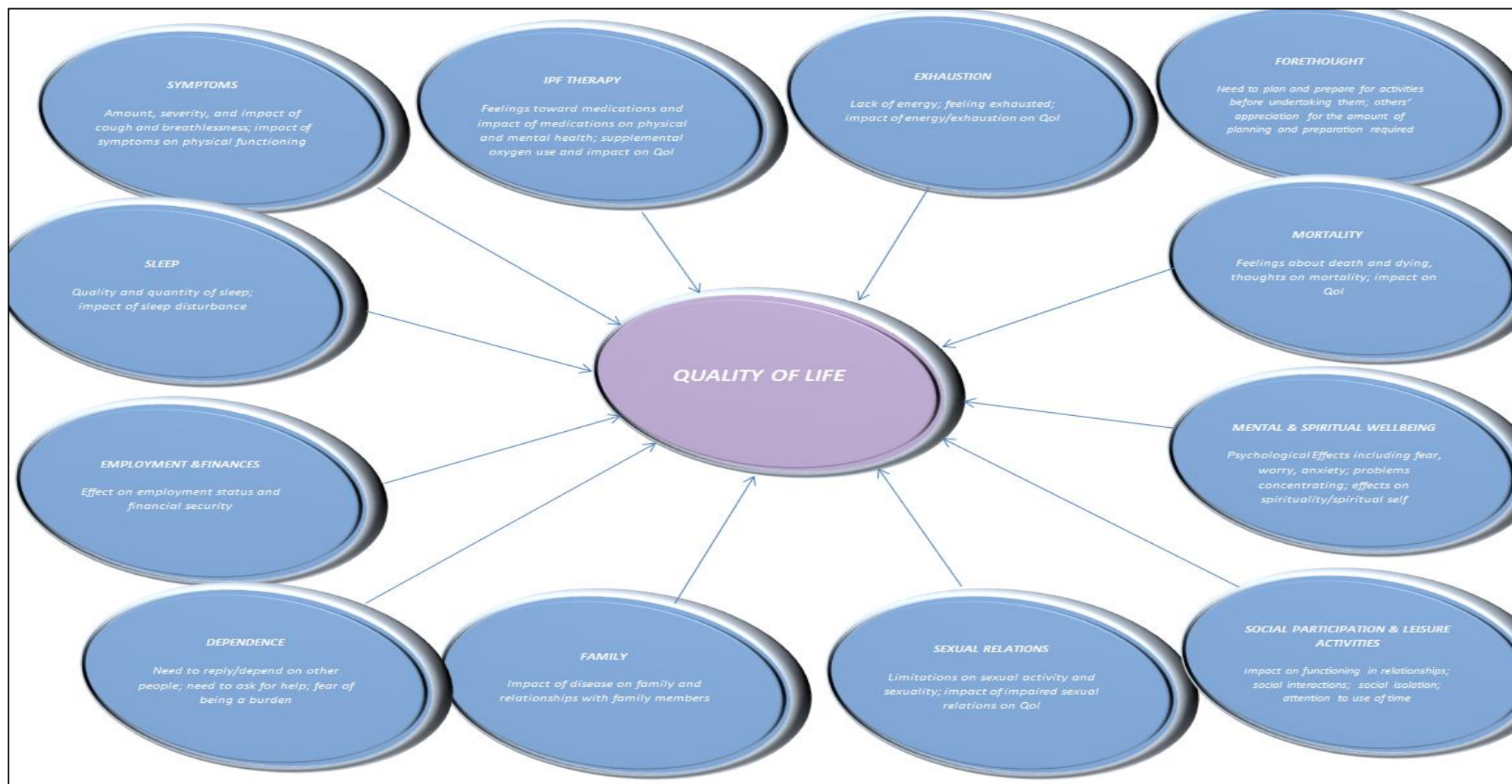


Figure 1-5 Diagrammatic representation of domains identified by Swigris et al for IPF patient (38)

1.7.2 Addressing concerns and information needs

Quantitative analysis of the perceptions of illness in IPF patients and their family members in one study is limited as numbers were small (N=32). However it observed that most patients understood their disease to be a 'serious condition' and that family members understood the patient might not survive (N=16).(39) In addition, a survey of 52 defined choice and open-ended questions of 1448 IPF patients and caregivers conducted in the United States reported that two thirds of respondents felt there was a clear lack of information at the time of diagnosis.(40) Schoenheit et al (36) found in their study of 45 European IPF patients interviewed, that the majority of participants had experienced delayed diagnoses and criticised the care they received, while a minority of participants who were diagnosed promptly reported their care more positively. Both groups reported rushed and insensitive diagnosis of IPF and that there was a lack of information provided to them about their disease. Qualitative methods have been shown to provide a richness of data and allow the researcher to delve deeply into issues which quantitative analysis may not allow.(41) In spite of this, there have been no qualitative studies to explore informal caregivers' information needs.

Research conducted in other non-malignant disease groups has identified that there is limited discussion between patients, informal caregivers and HPs directly addressing patients' and informal caregivers' concerns.(42, 43) This in turn has been shown to affect psychological morbidity.(44) A 2004 study in COPD patients observed that although most patients knew the name of their condition, over half wanted more information.(45) Research into satisfaction with communication and care in PIF-ILD has not been conducted.

1.8 Retrospective review of medical notes

To gain some preliminary understanding of the palliative care needs of PIF-ILD patients, I conducted a retrospective review of medical notes of deceased PIF-ILD patients for patients dying in a one year period. Approval for this piece of work was obtained from both the Royal Brompton and King's College NHS Foundation Trusts audit committees and protection of patient information was in line with each trusts' policy.

The two very different study settings were chosen to allow assessment of palliative care needs and end of life preferences of PIF-ILD patients from different cultural, socio-economic groups and two distinct ILD centres. This piece of work forms background work for the *identifying/developing theory* stage of the MRC guidance. The published paper is presented followed by a summary of the findings.

- 1.8.1 **Bajwah S, Higginson IJ, Ross JR, Wells AU, Birring SS, Patel A, Riley J. Specialist palliative care is more than drugs: a retrospective study of ILD patients. Lung 2012;190(2):215-20**

Specialist Palliative Care is More Than Drugs: A Retrospective Study of ILD Patients

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Abstract

Background This study aimed to assess the palliative care needs of progressive idiopathic fibrotic interstitial lung disease (PIF-ILD) populations in two London ILD centres.

Methods Patients' records from Royal Brompton Hospital (RBH) and King's College Hospital (KCH) were extracted to assess palliative care needs, use of palliative treatments, and whether end-of-life preferences were documented and achieved.

Results Forty-five PIF-ILD patients were identified (26 RBH, 19 KCH). Patients at RBH were younger (37–81 years, median = 61 years) and predominantly white British (23/26) compared to KCH's older, more racially diverse population (70–99 years, median = 82 years, 6/19

nonwhite). Seventeen of 45 patients had specialist palliative care team involvement. Nearly all patients (42/45) experienced breathlessness in their last year of life. Additional symptoms included cough, fatigue, depression/anxiety, and chest pain. All patients given opioids (22/45) or benzodiazepines (8/45) had documented benefit. Non-pharmacological treatments were rarely used. Few patients had preferred place of care (8/45) or preferred place of death (6/45) documented.

Conclusions Despite demographic variation, the patient populations at the two hospitals experienced similar symptoms. There was use of standard pharmacological treatments with symptom benefit. Nonpharmacological interventions were seldom used and documentation of preferred place of care and preferred place of death was poor.

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Keywords Cough · Dyspnoea · Lung disease · Interstitial · Pain · Palliative care · Pulmonary fibrosis

Introduction

There are at least 2,000 new cases of progressive idiopathic fibrotic interstitial lung disease (PIF-ILD) each year in England and Wales, with a similar number of deaths [1, 2]. There is evidence from death certificate data that the incidence is increasing [1, 2]. Median length of survival from diagnosis in the UK is ~3 years [3, 4] which is not dissimilar to that of lung cancer. Only a minority of patients are suitable for lung transplantation and there are no other significant treatment options once the disease has become advanced and irreversible [5].

The World Health Organisation defines palliative care as “an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening

illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual". The treatments involved in specialist respiratory palliative care contain both pharmacological (e.g., opioids, benzodiazepines and O₂ therapy) and nonpharmacological methods (e.g., counselling, relaxation/breathing therapies, use of hand-held fans, and spiritual care). When appropriate, specialist palliative care teams routinely address end-of-life planning needs. This includes assessing and documenting a patient's wishes on preferred place of care (the setting in which care should be delivered in the last days/weeks of life) and preferred place of death (where the patient prefers to die). Palliative care aims to facilitate the achievement of preferred places of care and death.

Palliative care has traditionally focused on improving quality of care in cancer. UK government strategies for individual disease groups [6, 7] and the recent End-of-Life Care Strategy [8] have highlighted the importance of developing effective palliative care interventions for patients with nonmalignant diagnoses. In addition, there is an increasing recognition of the need to improve palliative care currently available to nonmalignant respiratory diseases such as COPD [9]. To date there has been a paucity of research that has explored the palliative care needs of patients with PIF-ILD [10–13].

This study forms part of a larger project to develop evidenced-based palliative care guidelines and a complex end-of-life intervention for patients with PIF-ILD. The aims of this study were to compare the palliative care needs, treatments, and end-of-life preferences of PIF-ILD patients.

Methods

Two large London hospitals that regularly treat PIF-ILD patients were approached to take part. Royal Brompton Hospital (RBH) is a specialist ILD centre in central London. The unit has one of the largest diffuse lung disease patient populations in the world with over 500 new referrals a year for patients with ILD from across London and the surrounding counties. Patients come from areas with varying palliative care services and community support teams. King's College Hospital (KCH) is a tertiary hospital with a specialist ILD clinic in the southeast of London. KCH serves a geographical area characterised by material and social deprivation in addition to a large population of black and minority ethnic communities. The area has a network of palliative care services, including inpatient hospices, community services, and hospital support teams, coordinated through the South London Palliative Care Network and other regionally based networks. The two very different study settings were chosen to allow

assessment of palliative care needs and end-of-life preferences of PIF-ILD patients from different cross-cultural, socioeconomic groups and two distinct ILD centres.

Retrospective assessment of case notes of PIF-ILD patients who died between January 2009 and May 2010 was carried out using a data extraction sheet noting demographics and type of disease. PIF-ILD diseases included nonspecific interstitial pneumonia (NSIP), idiopathic pulmonary fibrosis (IPF), usual interstitial pneumonia (UIP), and idiopathic interstitial pneumonia (IIP) as classified and diagnosed by ATS/ERS criteria [14, 15]. We have concentrated on diagnoses that are idiopathic in nature and excluded pulmonary fibrosis related to drugs and occupational exposure.

The following specialist palliative care domains were used: palliative care needs (shortness of breath, cough, fatigue, insomnia, depression/anxiety, spiritual, and other), palliative treatments (opioids, benzodiazepines, steroids, antireflux agents, antidepressants, fan, relaxation therapy, counselling, referral for spiritual care) palliative care involvement, and end-of-life planning (preferred place of care and death). The data extraction sheet was piloted on ten sets of notes. The data were transferred to Statistical Package for the Social Sciences (SPSS; IBM, Chicago, IL) for analysis. The general practitioner was contacted for clarification of demographic information when necessary.

Results

Forty-five PIF-ILD patients were identified (26 RBH, 19 KCH). Clinicians had diagnosed PIF-ILD using ATS/ERS criteria 2002 [15] and IPF using ATS/ERS 2000 criteria [14]. The diagnoses were made initially on history, physical examination, chest radiograph, and lung function tests. Patients with possible IIP underwent high-resolution computed tomography (HRCT). If the HRCT test was consistent with features of IPF, then a diagnosis of IPF was made. If HRCT was inconsistent with IPF or inconclusive, surgical lung biopsy was performed. Overall, 34 patients underwent diagnostic biopsy.

Patients at RBH were younger (range = 37–81 years, median = 61 years) and predominantly white British (23/26) compared to KCH's older and more racially diverse population (range = 70–99 years, median = 82 years, 6/19 nonwhite).

The majority of patients had IPF (62% RBH, 90% KCH). Nine patients at RBH and 11 patients at KCH did not have any other significant comorbidities. Of the remaining patients, many had multiple comorbidities (Table 1).

There were no significant differences in other results between the two hospitals and the remaining data are therefore given for the total cohort.

Table 1 Characteristics of ILD centres and demographics of patients (obtained from records and clarified where necessary with general practitioner) with type of ILD and comorbidities documented

	RBH	KCH
Geographical catchment	London and surrounding counties	South East London
No. of referrals per annum	500	
Sex		
Male	14 (54)	10 (53)
Female	12 (46)	9 (47)
Age	61 ± 11	83 ± 8
Ethnicity		
White British	23 (88)	13 (69)
Indian	2 (8)	1 (5)
Bangladeshi	1 (4)	0
Black African	0	1 (5)
Black Caribbean	0	4 (21)
Type of ILD		
NSIP	8 (31)	1 (5)
IPF	16 (62)	17 (90)
UIP	0	1 (5)
Other ^a	2 (8)	0
Comorbidities		
Heart failure	2 (8)	4 (21)
COPD	4 (15)	3 (16)
GORD	8 (31)	1 (5)
Lung cancer	1 (4)	1 (5)
Renal failure	1 (4)	1 (5)
Pulmonary embolism	3 (12)	1 (5)
TB	2 (8)	0

Data presented as *n* (%) and mean ± SD

RBH Royal Brompton Hospital, KCH King's College Hospital, ILD interstitial lung disease, NSIP nonspecific interstitial pneumonia, IPF idiopathic pulmonary fibrosis, UIP usual interstitial pneumonia, COPD chronic obstructive pulmonary disease, GORD gastro-oesophageal reflux disease

^a One patient had a diagnosis of pleuroparenchymal fibrosis of unknown aetiology and one patient had a diagnosis of diffuse fibrotic lung disease on a background of serological autoimmune features

Table 2 Documentation of symptoms and psychological and spiritual needs

Shortness of breath	42 (93)
Cough	27 (60)
Fatigue	13 (29)
Insomnia	3 (6)
Depression/anxiety	10 (22)
Spiritual distress	0
Anorexia/weight loss	8 (18)
Chest pain	13 (29)
Generalised pain	4 (9)
Dyspepsia	2 (4)
Polyuria/polydipsia	2 (4)
Headaches	1 (2)
Diarrhoea	1 (2)
Dysphagia	1 (2)

Data presented as number of patients experiencing (%)

Table 3 Documentation of possible palliative treatments given and their effectiveness

	Patients receiving	Documentation of effectiveness		
		Effective	Not effective	No documentation
Opioids	22 (49)	21 (95)	0	1 (5)
Benzodiazepines	8 (18)	7 (88)	0	1 (12)
Steroids	37 (82)	22 (59)	10 (27)	5 (14)
Antireflux agents	3 (7)	2 (67)	1 (33)	0
Antidepressants	2 (4)	2 (100)	0	0
Fan	0	0	0	0
Relaxation therapy	1 (2)	1 (2)	0	0
Counselling/psychological support	3 (7)	3 (100)	0	0
Spiritual care support	0	0	0	0

Data presented as *n* (%)

Thirty-three of 45 patients had pulmonary function tests recorded. Percentage predicted transfer factor values were recorded, with a mean of 28% and a standard deviation of 12%. Patients had both a mean and median number of three symptoms. Nearly all patients experienced breathlessness in their last year of life (42/45, 93%). Additional symptoms included cough, fatigue, and depression/anxiety. Just under one third of patients experienced chest pain (Table 2).

The majority of patients received steroids, with symptomatic benefit documented in two thirds of patients. Opioids or benzodiazepines were given less frequently (22/45 opioids, 8/45 benzodiazepines). However, when drug

use was documented, they were found to be 100% effective, i.e., there was a documented improvement in symptom response. Nonpharmacological palliative treatments (fan, complementary therapy, but not oxygen) were rarely used (Table 3).

Few patients had a preferred place of care (8/45) or a preferred place of death (6/45) documented. The majority of patients died in the acute hospital setting (34/45). 17 (38%) patients had some sort of specialist palliative care team (PCT) involvement. Of those, 4 (9%) had both hospital and community palliative care teams involved in their care. 28 (62%) did not have any palliative care input in the last year of life (Table 4).

Table 4 Documentation of preferred place of care and death compared to actual place of death with specialist palliative care involvement

Preferred place of care	
Home	5 (11)
Hospice	2 (4)
Hospital	1 (2)
Not documented	37 (82)
Preferred place of death	
Home	1 (2)
Hospice	4 (8)
Hospital	1 (2)
Not documented	39 (87)
Actual place of death	
Home	4 (8)
Hospice	5 (11)
Hospital	34 (76)
Unknown	2 (4)
Palliative care involvement	
No palliative care	28 (62)
Hospital palliative care only	5 (11)
Community palliative care only	8 (18)
Both hospital and community palliative care	4 (9)

Data presented as n (%)

Discussion

This study allowed the palliative care needs and treatment of patients with PIF-ILD to be examined. Patients from the two hospitals were very different demographically, with older and more ethnically diverse patients at KCH. Patients from KCH were more likely to have received a diagnosis of IPF than at RBH. This may reflect an increased tendency at RBH to confirm PIF-ILD diagnosis via lung biopsy. Despite the demographic differences, there was very little difference in the palliative care needs of these patients.

Previous literature has noted that PIF-ILD patients suffer from many symptoms, including shortness of breath, cough, low mood, and fatigue [10–13] and this was supported by our study. Unsurprisingly, shortness of breath was the most prevalent symptom. However, the prevalence of chest pain in these patients was unexpected. It is not clear whether these symptoms are directly related to ILD or the comorbidities such as pulmonary embolisms experienced. In our study, even though the mean number of palliative care needs experienced in the last year of life is small, it is likely that this has been underestimated. Justice et al. [16] found that compared to self-report, clinicians significantly underreport the presence and severity of symptoms. Pulmonary function tests were carried out. However, as this was a retrospective review of case notes,

it is not possible to relate pulmonary function tests more closely to severity of symptoms.

There appeared to be a failure to consider wider issues in the palliation of these patients. There was no documented assessment of spiritual needs and rarely documentation of assessment for depression and anxiety. It is unlikely that these issues do not occur in this group of patients. A previous study by Edmonds et al. [17] suggests that patients with chronic lung disease at the end of life have physical and psychosocial needs at least as severe as patients with lung cancer. A systematic review by Solano et al. [18] found a similar prevalence of patients experiencing pain in cancer, heart disease, and COPD compared to our study population. In addition, comparable levels of fatigue and insomnia were found in cancer populations and anorexia in heart disease (HD) patients compared to our PIF-ILD patients (Table 5). Of note, our study population experienced more breathlessness than that experienced in the cancer, AIDS, heart disease, COPD, or renal disease (RD) population reviewed by Solano et al. [18]. Our study is limited by the reliance of health professionals recognising the importance of asking about wider palliative care needs, patients reporting them, and health professional documentation. It is likely that the palliative needs of these patients are actually greater than reported in our study and span a much wider range.

The paucity of documented use of nonpharmacological therapies such as counselling and relaxation therapy was marked. It is possible that there is little recognition of the effectiveness of these interventions in improving symptom control. Alternatively, this may reflect a “sticking-plaster” palliative approach in which there is an earnest attempt by the respiratory teams to deal with the cardinal and expected symptoms (i.e., dyspnoea) with standard pharmacological intervention (opioids and/or benzodiazepines in addition to oxygen therapy). In our study, both units have been attempting to address this, although the approach appears

Table 5 Prevalence of palliative care needs of both hospitals compared to cancer, AIDS, HD, and RD as found by Solano et al. [18]

	Combined RBH + KCH	Cancer	AIDS	HD	COPD	RD
Shortness of breath	98	10–70	11–62	60–88	90–95	11–62
Fatigue	29	32–90	54–85	69–82	68–80	73–87
Insomnia	7	9–69	74	36–48	55–65	31–71
Anorexia/ weight loss	18	30–92	51	21–41	35–67	25–64
Pain	36	35–96	63–80	41–77	34–77	47–50

Data presented as %

to be far from systematic. Expert palliation or specialist palliative care aims to use both pharmacological and nonpharmacological therapies in a systematic way in the palliation of both expected and unexpected symptoms. However, there is a need for clear evidenced-based guidelines on how the palliative care needs of patients with PIF-ILD should be managed.

Recent governmental strategies [8] have encouraged the achievement of preferred place of care and death for patients at the end of life. However, our study shows poor documentation of both. It is difficult to comment on whether preferred place of death is achieved. However, previous studies have shown that the majority (49–78%) of patients would rather die at home [19]. In our study, the majority of patients died in hospital. It is possible that discussions on end-of-life preferences are occurring with the patients, although Curtis et al. [9] found that patient–physician communication about end-of-life care was unlikely to occur in COPD patients. Without clear documentation and communication across primary and secondary healthcare settings, achievement of preferred place of care and preferred place of death is unlikely to occur in PIF-ILD patients. Only when end-of-life preferences are clearly documented and assessment of whether these are achieved is conducted will we be able to start to investigate and rectify possible contributing factors.

The majority of PIF-ILD patients did not have any palliative care input in their last year of life. However, our study may highlight and reflect the previous difficulty of defining when these patients were entering the preterminal phase. Respiratory physicians may have found it difficult to address end-of-life issues without an accurate poor prognosis. However, future development of effective staging instruments [20] should allow physicians to identify PIF-ILD patients in the last year of life.

Very few patients had both community and hospital palliative care team support. These patients often had multiple admissions to the acute setting in the last year of life (RBH inpatient records 2009) and it is possible that they may have benefitted from both community and hospital palliative care input in addressing symptom control, preventing hospital admission, and achieving end-of-life preferences. There is evidence that palliative care teams improve outcomes (symptoms, therapies offered) for patients with cancer and may reduce healthcare costs by transferring care from acute hospital to community settings [21]. We advocate a proactive approach for PIF-ILD patients that involves systematic and holistic palliation by respiratory physicians whilst supported by specialist palliative care teams. However, access to such support is not routinely offered to patients with conditions other than cancer, where the effects of palliative intervention are not well understood and indeed the models for

cancer may not directly apply. In addition, it is not clear whether other reasons such as monetary, religious/cultural, or health professionals' perceptions of palliative care may prevent referral in this group and it was beyond the scope of this study to assess this. There is an urgent need for further research into the palliative care needs and preferences of the ILD population and to develop interventions that enable patients to die in their preferred place of death.

There are a number of limitations to our study. As it is a retrospective review of case notes, we are reliant on health professionals recording symptoms and the effectiveness of palliative interventions. It is likely that symptoms have been underreported. On the other hand, effectiveness of interventions was recorded in our study only when there was a clear positive effect documented in the clinical notes. It is possible that interventions were being used without being recorded or they were effective and it was not documented. In addition, there were no validated outcome measures used in the assessment of the palliative care needs of these patients which is a clear learning point. It is difficult to believe that we will be able to deliver effective interventions to improve symptom control when they are not being assessed using a systematic and validated method. Finally, even though palliative care involvement was noted, the level of palliative care input was not recorded for this study. It is possible that some patients had more intensive palliative care support than others and more detailed recording of this should be considered in any similar future studies.

Conclusion

Despite demographic variation between sites, the patient populations were documented as experiencing similar symptoms. Pain was more prominently documented than previously noted in the literature. There was documented use of standard palliative pharmacological treatments with symptom benefit despite limited specialist palliative care involvement. The numbers documented as having a beneficial response to symptoms with these interventions is encouraging and needs further quantification. Nonpharmacological interventions were seldom documented as being used, and documentation of preferred place of care and preferred place of death was poor.

These results may reflect difficulty in identifying and managing a preterminal phase in this group of patients and/or a need for increased access to specialist palliative care services.

Conflict of interest The authors have no conflict of interest to disclose.

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This review showed that these patients experience:

- **A high symptom and psychological burden in the last year of life:**

Nearly all patients (42/45) experienced breathlessness in their last year of life. Additional symptoms included cough, fatigue, depression/anxiety and chest pain.

- **Non-pharmacological treatments were rarely used.**

All patients given opioids (22/45) or benzodiazepines (8/45) had documented benefit but non-pharmacological treatments were rarely used.

- **Limited palliative care involvement**

Despite having a large amount of uncontrolled symptoms, only 17/45 had palliative care team involvement in the last year of life.

- **Limited documentation of end of life preferences**

Few patients had preferred place of care (8/45) or preferred place of death (6/45) documented.

In developing a palliative care intervention at the end of life for PIF-ILD patients, an intervention would need to address the symptom control needs of patients, involve palliative care services and document end of life preferences. However, as this is a retrospective review of clinical notes any findings from this piece of work must be treated cautiously.

1.9 Theoretical model of H2H for PIF-ILD

This section will form the *identifying/developing theory* phase of the development stage of the MRC framework.(13) In considering a theoretical model of H2H which may be appropriate for PIF-ILD patients and which may meet their palliative care needs, I will first appraise what the most appropriate definition of need is, its context in health care and its relevance to PIF-ILD palliative care. I will then use this definition and integrate it with previous work examining factors affecting the QoL of these patients and the new *identifying/developing theory* work I have conducted in this chapter to develop a theoretical model of H2H for advanced PIF-ILD patients and their informal caregivers.

1.9.1 Definitions of need

Need is a multi-faceted concept with no one universal definition. Sociologists such as Bradshaw (46) have proposed a taxonomy of need. Here he defines “normative need” as an expert’s definition of need in a given situation. “Felt need” is equated with “want”, expressed as a lay person’s own assessment of his or her requirement for health. “Expressed need” or demand is felt need converted into action, by seeking assistance, either by use of services or request for information. “Comparative need” is assessed by comparing the services received by different people with similar characteristics. If some and not others have received care, then there is a comparative need in those not receiving it.

Philosophers such as Baldwin(47) have proposed a 'tension need' which implies a desire to compensate for some dis-equilibrium such as thirst due to fluid loss. He also proposed a 'teleological need' reflecting the gap between actual and desired status. In addition Maslow proposed a hierarchical definition of need in which basic needs (food and water) progress upwards through safety needs, belonging needs, and esteem needs and culminate in self-actualisation.(48) Maslow argues that as the basic needs are met, the higher needs become more important.(49, 50). However, this may be too simplistic as higher needs may be important even when basic needs are not met. For example existential suffering may be considered a higher need which warrants attention from palliative care professionals as it may be inextricably linked to basic needs such as pain control. This higher need does not necessarily become more

important as basic needs are met. In fact the basic need of effective pain control may never be met unless the higher existential needs are.

1.9.2 **Health and healthcare needs**

Pragmatically, Carr and Wolfe (51) describe an aspect of health needs which they term as “unmet need”. This is the difference, if any, between the health care judged to be needed and the healthcare actually provided. According to Sheiham et al (52), true treatment need may lie somewhere between the objective (assessed by a doctor) and subjective (assessed by the patient). Donabedian (53) describes need as a state of being that creates a requirement for care and therefore represents a potential for use of health services.

However, the need for healthcare should be distinguished from the need for health. The need for health is broader (incorporating the wider social and environmental determinants of health such as deprivation, housing etc (54)) and can include problems for which there is no known treatment.

Within the NHS, healthcare needs are defined as those that can benefit from health care ie that a need for healthcare exists when an individual has an illness or disability for which there is effective and acceptable treatment or care.(55) The benefit may not just be a change in clinical status or cure but can include reassurance, supportive care and the relief of informal caregivers.(56) However, this definition implies that the need for healthcare only exists if there is capacity to benefit from a particular healthcare service. The onus here is on the outcome “capacity to benefit”.(55)

This definition has some problems when applied to this PIF-ILD group of patients. Firstly, the benefit of healthcare may be affected inversely by the severity of the disease. For example, a patient with advanced PIF-ILD may “benefit less” from receiving cardiac surgery compared to a patient without PIF-ILD who may have many years to live post-surgery. How “capacity to benefit” is defined becomes very important. Secondly, if there isn’t an effective intervention for a healthcare need, this definition would imply that there is no longer a healthcare need. In essence, if there is no solution or appropriate supportive care available, the problem is ignored. This definition of healthcare need could be used to justify refusing patients treatment or care

rather than focussing on the very real health needs of populations. The “capacity to benefit” as an outcome measure differs from health care needs and is discussed in detail by Culyer.(57) These two concepts are measurable in different ways which do not necessarily match.(55) PIF-ILD palliative care is an under-researched area for which there are few interventions available to improve symptoms and QoL. In addition there is little knowledge on how supportive care ought to be delivered to these patients and informal caregivers. Applying the NHS definition of need could imply that as there are few effective/acceptable interventions available, PIF-ILD patients do not have symptom control/QoL health care needs.

In a similar vein, Buchan et al defined health service needs as *‘those for whom an intervention produces a benefit at reasonable risk and acceptable cost’*.(58) This definition incorporates effectiveness *and* cost-effectiveness and is the one favoured by health economists. However, by this definition, if an intervention does not result in benefit or does result in a benefit but at unreasonable cost, there is no health service need. Again, this would not be appropriate for PIF-ILD palliative care.

1.9.3 **The concept of need in palliative care**

Another way of defining need is:

‘the requirement of individuals to enable them to achieve, maintain or restore an acceptable level of social independence or QoL, as defined by particular care agency or authority’ .(59)

This definition does not negate healthcare needs (including specialist palliative care needs) if there isn’t an effective or reasonably priced intervention available or if the interventions available are unable to improve the need. However, there are a number of problems with this definition. Social independence does not necessarily equate to need. A patient may have acceptable social independence and have a number of needs. Conversely, terminal patients may have very little social independence but not necessarily have a large number of needs. In addition, an acceptable level of QoL ought to be defined by the patient, not a “particular agency/authority”. However, improving QoL through holistic assessment and treatment of the patient and informal caregiver is integral to the WHO definition of palliative care(20) (which I believe is fundamental to the practice of palliative care). Therefore, QoL as defined by the

patient (and measured through appropriate methods), ought to be an integral part of any definition of need. It may be argued that QoL may be functionally driven. However, in this group of patients, work done by Swigris et al (38) has shown that patient's perspectives of how their disease affects the QoL is multi-factorial with physical, psychosocial and spiritual components.

Therefore the definition of need which I have built and will be using for this group of patients and informal caregivers will be:

'The requirement of individuals to enable them to achieve, maintain or restore an acceptable level of QoL as defined by the individual. '

In using this definition, I am not proposing that we ignore the effectiveness/possible cost implications of interventions used in PIF-ILD palliative care (as this is important for translation of the work clinically). However, I do not believe that these factors should have any importance in defining a need (and more specifically a specialist palliative care need) in PIF-ILD. This definition also links to the WHO definition of palliative care which focusses on improving the QoL of patients and their families through holistic means but importantly leaves the onus of defining QoL with the patient. The different definitions of need and their application to palliative care are contrasted in Table 1-2 Page 94.

Table 1-2 Table summarising different definitions of need and their application to palliative care

	Type of need	Definition	Examples in palliative care	Pros	Cons
Sociological (46)	Normative	Need that is defined by experts	Decision that a patient requires a syringe driver to control symptoms	Explicit standard applied consistently and fairly	May be paternalistic and arbitrary and thresholds manipulated to manage “unmet need”
	Felt	Need perceived by individual	Completion of patient palliative care outcome scales such as POS	Affirms the patient’s definition of need	Felt needs are limited by individual perceptions and knowledge of services
	Expressed	Felt needs taken into action. Help seeking.	Patients and informal caregivers requesting input and support from community palliative care services	More testing of the commitment of the individual to do something about meeting their needs	Smaller proportion in need than might be. Excludes all those unaware that a service exists.
	Comparative	Individuals with similar characteristics to those receiving help	Compiling a list of palliative care patients in need of specialist palliative care support based on characteristics which have been associated with high palliative care needs in the past.	An easy case for parity of provision can be established	Based on experience.
Philosophical	Tension(47)	Desire to compensate for some dis-equilibrium	Breathlessness due to large volumes of ascites	Recognises the symptoms experienced by the patient	Limited by HP’ knowledge and ability to recognise.
	Teleological (47)	The gap between actual and desired status	The desire for palliative brain radiotherapy for brain metastases to improve symptom control and longevity of life	Recognises what the patient deems important for their symptom control and QoL	Smaller proportion in need than might be. Excludes all those unaware that a service exists.
	Hierarchy (48)	Need in which basic need (eg food and water) progress upwards through safety needs, belonging needs, and esteem needs and culminate in self-actualisation	(1) distressing symptoms, such as pain or dyspnea;(2) fears for physical safety, of dying or abandonment; (3) affection, love and acceptance in the face of devastating illness; (4) esteem, respect, and appreciation for the person; (5) self actualisation and transcendence.(60)	Allows comprehensive assessment of physical, psychosocial and spiritual need	May be overly simplistic linear model (not necessary that lower order needs be met before higher level needs can be addressed)
Pragmatic	Unmet (51)	Healthcare judged to be needed and healthcare actually provided	Patients judged to require community palliative care support but this is not possible due to poor staffing levels	An easy case for parity of provision can be established directing allocation of resources for the future	Does not prioritise the patient’s concerns. Likely to be smaller proportion in need than might be.
NHS(61)	Healthcare need	Need for healthcare exists when there is capacity to benefit from an intervention	Breathlessness which is opioid responsive	Outcomes of health interventions become more important and there is greater focus on developing effective interventions. “Benefit” may be comfort or reassurance.	Capacity to benefit is not fixed and is subject to current knowledge, current research agenda and the effectiveness of interventions. Need is ignored if there is not an effective intervention
Health economic(58)		Health care needs are those for which an intervention produces a benefit at a reasonable cost	Expensive palliative chemotherapies which have few side effects and are effective in terms of symptom control and QoL but are only successful in the very few	Ethically we must consider justice in allocation of finite resources within the NHS	Ignores health service needs for which there are only expensive (ie unreasonable costing) interventions available
Proposed definition for PIF-ILD palliative care		The requirement of individuals to enable them to achieve, maintain or restore an acceptable level of QoL as defined by the patient	Developing complex palliative care interventions at the end of life aimed at improving the palliative care needs (as defined by WHO) of patients and informal caregivers with PIF-ILD.	This definition does not negate healthcare needs (including specialist palliative care needs) if there isn’t an effective or reasonably priced intervention available or if the interventions available are unable to improve the need. Onus is on patient to define QoL.	Ignores practical and ethical implications of having to meet needs where there are only expensive interventions available

1.9.4.1 Integrating care

Integration has been described as the “glue” that bonds organisations together, thus enabling them to achieve common goals.(62) Integrated care “seeks to improve the quality of care for individual patients, service users and informal caregivers by ensuring that services are well co-ordinated around their needs”.(63) Integrated care has been described as necessary for any individual for whom a lack of co-ordination of care leads to an adverse impact on care experience and outcomes.(63)

In its June 2011 summary report, the NHS Future Forum called for the commissioning of integrated care for patients with long-term conditions, complex needs, and at the end of life.(64)

In addition, the NICE quality standard for IPF states:

“.....services should be commissioned from and coordinated across all relevant agencies encompassing the whole idiopathic pulmonary fibrosis care pathway. A person-centred, integrated approach to providing services is fundamental to delivering high-quality care to adults with idiopathic pulmonary fibrosis.”(65)

In considering whether to use integrated care for patients at the end of life and specifically for patients with PIF-ILD, examples of integrated care across different healthcare settings with relevance to PIF-ILD need to be considered (Table 1-3 Page 96).

Table 1-3 A table to show the positive effects of integrated care and their possible relevance to PIF-ILD

Examples of Integrating care	Methods	Positive effects	Relevance for PIF-ILD
Care for older people in Torbay(66)	Care delivered through integrated teams of health and social care staff. Budgets were pooled and used flexibly by teams who were able to arrange and fund services to meet the specific needs of older people.	Increased spending on intermediate care services enabled older people to be supported at home and helped avoid inappropriate hospital admissions. Results included a reduction in the daily average number of occupied beds and a reduction in emergency bed day use.	Many PIF-ILD patients are elderly with unnecessary hospital admissions. Integrating and individualising care delivered may help prevent hospital admissions.
Diabetes care in Bolton (67)	A team of community-based diabetes specialists worked with the local hospital for inpatient care and with general practices to provide support and undertake shared consultations.	High satisfaction levels and the lowest number of hospital bed days per person with diabetes in the Greater Manchester area were reported.	Many ILD services are specialist services. Education and easy access to advice from ILD services may reduce hospital bed days.
Chronic care management in Wales (68)	Three Health Boards pioneered strategies to co-ordinate care for people with multiple chronic illness. By employing a 'shared care' model of working between primary, secondary and social care – and investing in multidisciplinary teams	There was a reduction in the total number of bed days for emergency admissions for chronic illness by an average of 19.5 per cent between 2007 and 2009. This represented an overall cost reduction of £2,224,201	PIF-ILD patients often have multiple co-morbidities. A 'shared care' model across primary, secondary and social care may reduce bed days for emergency admissions for PIF-ILD.

Many factors in the health care setting have been described which inhibit integration of healthcare. These include inter sector boundaries between different healthcare settings, divisions between different members of the multi-disciplinary team and initial costs for staff, support systems and services. (62) On an international level, problems of co-ordination and continuity of care are experienced when patients transition between acute curative care and long term/end of life care. This is more likely to be the case if curative and long term care/end of life care are financed and regulated by different organisations. (69)

1.9.4.2 Care planning

The National Service Framework for patients with long term conditions (70) focuses on people with long term neurological conditions but much of the guidance it offers can apply to anyone living with a long-term condition eg PIF-ILD. It offers people as part of a quality requirement a full assessment of their health and social care needs. In addition they are offered information and education about their condition; the chance to make decisions about their treatment; and to be involved in writing a plan about how their care needs will be met (a care plan). There is a requirement to deliver a patient-centred service which focuses on a holistic, integrated, interdisciplinary approach to care planning, review and service delivery involving a range of agencies. The onus is on local NHS and social services to ensure they meet this requirement. It is also identified in the NSF that some people with more complex needs requiring skilled multi-disciplinary input from a number of different agencies will need an identified person who co-ordinates care.

Care planning may provide a framework to support the policy imperative of 'no decision about me without me' prioritised in the 'Equity and Excellence: Liberating the NHS (2010)'(71) , and the delivery of shared decision making. It aims to provide a gateway for the delivery of choice through personalisation of care.

1.9.4.3 Integrated care planning and palliative care

In 2008 the NHS developed the *End of Life Care Strategy* (11) which recognised that the quality of care at the end of life was generally variable and the strategy was to bring about a stepped change. Key recommendations included:

- development of care plans that reflect people's needs, wishes and preferences that are reviewed as circumstances change and are available across different healthcare settings.
- co-ordination of care in accordance with the care plan and the delivery of high-quality services across all sectors and at all times.

In the examples shown previously (Table 1-3 Page 96), integrated care may improve patient care, resulting in improved patient satisfaction, making services more efficient, reduce hospital admissions and save the NHS money. In addition, care planning may provide a tool to meet patients' and informal caregiver's needs and wishes at the end of life. It has been proposed that to achieve integrated care planning, those involved with planning and providing services must impose the user's perspective as the organising principle of service delivery (72, 73) and that this is a negative and time consuming concept. However, the opposing and stronger argument is that integrated care approach with the individualised care planning encourages more holistic and personalised approaches to multi-dimensional health needs.(74) This is certainly important at the end of life and should be encouraged for palliative care patients including PIF-ILD patients and informal caregivers who may have considerable unmet needs and who may experience an adverse impact on care experience and outcomes as a result of lack of co-ordination of care.

1.9.4.4 Co-ordination of care

PIF-ILD patients are often seen in specialised centres. During the early stages of the disease, patients and informal caregivers may become reliant on specialist care. In addition, there may be poor communication with primary healthcare professionals and a deskilling of community HPs on how to manage these diseases. Conventional care systems were proposed and intended to treat people with acute illnesses and therefore required little co-ordination of care.(75) These systems are adequate for early PIF-ILD (where the focus of care is in the

specialist centre). Conversely, the management of patients with complex conditions (such as PIF-ILD) at the end of life requires cooperation between disciplines across multiple healthcare settings. However, when patient care is shared between primary, secondary or tertiary settings, evidence has identified significant problems in team coordination and communication.(76) Targeted organisation of care with improvement in co-ordination and communication is required to enable appropriate delivery of palliative care (77) for these patients and informal caregivers.

1.9.4.5 A model of integrated care planning for PIF-ILD

The term “specialised palliative care” refers to a service model that incorporates coordination and support for clinicians (GPs, ILD physicians etc) and for other services (district nursing) and management of patient and family concerns. Holistic care underpins a palliative approach; encompassing the physical, social, psychological and spiritual dimensions as defined by WHO.(20)

The End of Life Care Strategy (11) also identified other key areas which may be important to PIF-ILD patients and their informal caregivers. These include:

- Identifying people approaching the end of life with emphasis on HPs' skills development in this area
- Rapid access to care that responds to a rapid change in a person's condition and that is available in the community 24/7, avoiding unnecessary emergency admissions and facilitating people to die in their place of choice.
- Involving and supporting informal caregivers, including the provision of information about the likely progress of a person's condition and services that are available.

Swigris et al (38) when developing a QoL tool, used focus groups and individual in-depth interviews with 20 idiopathic pulmonary fibrosis (IPF) patients to collect their perspectives on how IPF affects their lives (with a focus on QoL). Swigris et al(38) analysed these perspectives and organised them into a conceptual framework consisting of 12 domains. A diagrammatic representation of the Swigris paper is found in Figure 1-5 Page 80

These domains have been used alongside the WHO model of palliative care with the underlying directions of the NSF framework for long term conditions and End of Life Care Strategy to develop the theoretical model underpinning the H2H intervention.

1.9.4.6 The CC model of care and Hospital2Home (H2H)

The management of patients with chronic and complex conditions relies heavily on cooperation between disciplines. Specialist services frequently use multidisciplinary team meetings to determine management. When patient care is shared between secondary or tertiary informal caregivers and community informal caregivers, evidence has identified significant problems in team coordination and communication.⁽⁷⁶⁾ Case conferencing involves a formal meeting between multi-disciplinary HP involved in care. The goal of case conferencing is to provide holistic, coordinated, and integrated services across providers improving co-ordination of care and communication.

There have been 2 randomised trials conducted looking at the use of the CC in the palliative care setting. Both of these have been conducted in Australia. The first of which was conducted by Mitchell et al.⁽⁷⁸⁾ This was a multi-centre RCT to assess whether telephone CCs between GPs and specialist palliative care teams (without the patient or informal caregiver present) improved patients' QoL and reduced the strain of caring for the informal caregivers compared to usual care. This trial randomised 159 cancer patients and found that the primary outcome-global QoL was not influenced by the intervention but the CC group showed better maintenance of physical and mental health measures of QoL in the 35 days before death. It was suggested that CCs may improve clinical relationships and care plans at referral but that these were not usually implemented until severe symptoms developed. There was a positive impact on caregiver burden with significantly lower carer burden in two of the five domains (impact on schedule and lack of family support) on the Caregiver Reaction Assessment ⁽⁷⁹⁾ as well as the total score. Subsequently, GPs who had participated in the CCs were interviewed by telephone and specialist palliative care teams were interviewed in focus groups. GPs reported that the CC allowed them to be better informed, made discharge planning easier and allowed clear delineation of role between the GP and the palliative care service.⁽⁷⁶⁾ Palliative care teams felt that the CC provided particular insight as to the GPs' willingness to provide after-hours care and house calls and knowledge of palliative care treatments. Both GPs and palliative care teams felt

that routine CCs were less useful than those held at critical points in the patient's illness (before discharge home or when there were complex issues). (76)

A second RCT also conducted in Australia, evaluated 3 interventions 1) a single CC between GP and the specialist palliative care team vs control 2) educational outreaching on palliative pain relief delivered to specific patients' GPs vs control and 3) education interventions on pain and other symptom management provided to the patient and primary carer, delivered by palliative care nurses vs control. A single CC was found to reduce hospitalisations rates by 0.5 per patient. CCs maintained a 10% improved performance status compared with normal care from 60 days after the CC until death. The greatest benefit in terms of performance status occurred when the patient could not manage without help. (80)

A fundamental difference between these studies and the H2H model is that the CCs in these 2 studies are built directly and explicitly around the GP, not around the patient and informal caregivers. In the Mitchell et al trial (78), patients and informal caregivers were not in attendance.

Figure 1-6 Page 102 shows the theoretical model of the H2H that I have developed and its possible mechanisms of effect in improving PIF-ILD patients' and their informal caregivers' disease journey.

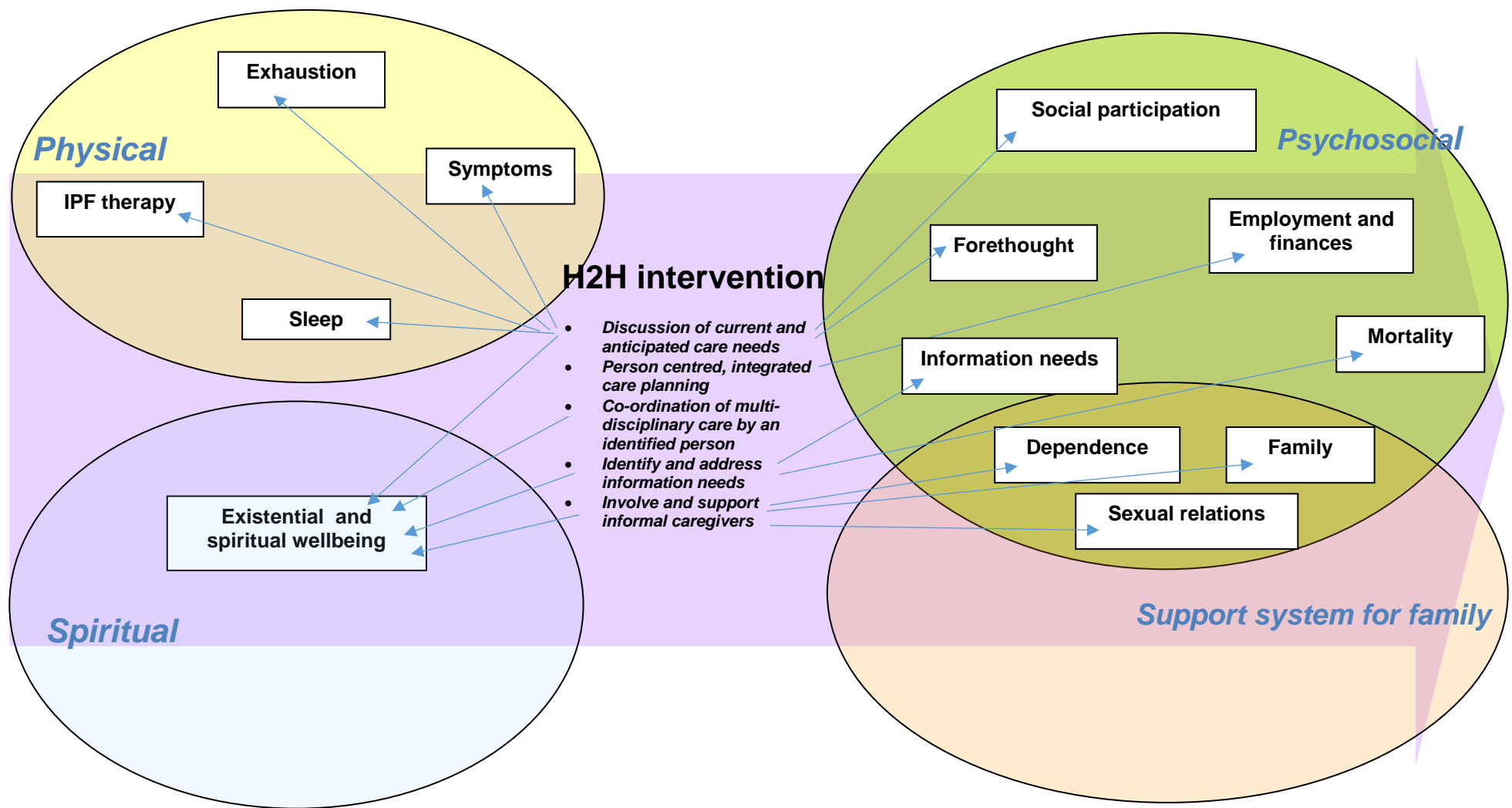


Figure 1-6 The proposed H2H PIF-ILD model and possible mechanisms of effect on the PIF-ILD patient and informal caregivers' disease journey

1.10 Conclusion

PIF-ILD is an irreversible disease with no effective treatment options. Patients experience a progressive loss of functional ability and ultimately die from acute respiratory failure. Despite awareness that PIF-ILD patients have specific palliative care needs, little primary research has been conducted to guide delivery.

The MRC guidance has been developed to guide researchers in developing and evaluating complex interventions. In addition the MOREcare statement is used when developing complex interventions at the end of life. The H2H CC model of care is a complex intervention which brings together the components of a CC with individualisation from a care plan. This model of care has not yet been used in the non-malignant setting. In developing and evaluating the H2H intervention for PIF-ILD patients and informal caregivers, the MRC complex intervention guidance supported by the MOREcare guidance has been used as the methodological approach.

This chapter forms part of the *identifying the evidence base* and *identifying/developing theory* phase of the MRC guidance. In this chapter, I found that there is a paucity of interventions focussing on symptom control and QoL. In addition, there is limited research into the palliative care needs of these patients. However, background work conducted as the retrospective review of medical notes/audit, shows that these patients have a high symptom burden in last year of life with limited palliative care involvement.

In addition, in this chapter I have appraised the most appropriate definition of need and more specifically healthcare need deciding that the most appropriate definition links to the WHO definition of palliative care and focusses on improving the QoL of patients and their families through holistic means but leaves the onus of defining QoL with the patient. I have discussed the advantages of integrated care- improvement in the quality of care for individual patients, service users and informal caregivers by ensuring that services are well co-ordinated around their needs. I have also discussed the possible advantages of the H2H CC for PIF-ILD which may include providing holistic, coordinated, and integrated services across providers improving co-ordination of care and communication. Finally, I have presented a theoretical model to describe the way in which H2H may work in the PIF-ILD setting. I will now go on to present the overall aims and objectives of this study followed by the methods.

Chapter 2 Aims and Objectives

2.1 Aims

The aim of this thesis is to develop and evaluate a complex intervention to improve the palliative care needs for those affected with PIF-ILD, by adopting the MRC complex intervention guidance as the methodological approach.

2.2 Objectives

1. To identify and describe specialist palliative care needs within this population.
2. To identify patients', informal caregivers' and HPs' perceptions on co-ordination of care, communication and information needs.
3. To identify patients', informal caregivers' and HPs' views on the H2H model of care and ways in which it may be improved/adapted for the PIF-ILD population.
4. To integrate the above findings from 1-3 to adapt an acceptable and accessible model of the H2H intervention.
5. To define appropriate outcomes and measures for the adapted H2H intervention.
6. To begin to evaluate H2H in a phase II study.
7. To evaluate the intervention in terms of feasibility and acceptability in a phase II study.
8. To use the above work to inform a future larger randomised controlled trial (RCT phase III/**Evaluation** trial).

Chapter 3 Overall methods

3.1 Introduction

This chapter presents a rationale for the use of mixed methods in this study. The detailed methods used for each component will be presented in their respective publications and chapters. This chapter focuses on how the MRC guidance will be used in developing and evaluating the H2H intervention, whilst supported by the MOREcare guidance, the rationale and the use of mixed methods and finally how integration of the mixed methods will be used within the MRC guidance.

3.2 Paradigm debates as applied to this study

Epistemology is “the study of the nature of knowledge and justification”.⁽⁸¹⁾ Research methodology is located in the philosophy of how we come to know things, that is epistemology.⁽⁸²⁾ In turn, methodology provides justification for the methods of a research project which produces data and analyses.⁽⁸³⁾ Qualitative and quantitative methods have been used with differing frequencies throughout the relatively short history of palliative care research.⁽⁸⁴⁻⁸⁶⁾ During the 2000s, qualitative methodologies gained increased momentum⁽⁸⁷⁾, perhaps raising the question of whether today these methodologies are moving towards the position formally occupied by quantitative methodologies. This concerns not only the precedence of one methodology over the other in terms of how often they are used, but also the relationship between the two approaches. Traditionally, qualitative and quantitative methods belong to different paradigms or worldviews that guide research ⁽⁸⁸⁾, and the relationships between the two have even been referred to as ‘battlefields of wars’. ⁽⁸⁹⁾ Purists argue that quantitative and qualitative methods stem from different ontologic, epistemologic and axiologic assumptions about the nature of research. ⁽⁸⁹⁾ Moreover, for purists, the assumptions associated with both paradigms are incompatible regarding how the world is viewed and what it is important to know. Purists, that include Smith ⁽⁹⁰⁾ and Smith and Heshusius ⁽⁹¹⁾, suggest that quantitative and qualitative approaches cannot and should not be mixed. This is referred to as the compatibility thesis. ⁽⁹²⁾ ‘Situationalists’ maintain the mono-method (paradigmatic) stance held by purists, but also contend that both methods have some intrinsic value. However, they believe that certain research questions lend themselves more to quantitative approaches, whereas other research questions are more suitable for qualitative methods. Therefore,

although representing very different orientations, the two approaches are treated as being 'complementary'.(93) Finally, at the other end of the continuum, 'pragmatists', unlike purists and situationalists, contend that a false dichotomy exists between quantitative and qualitative approaches.(94) These proponents believe that quantitative methods are not necessarily positivist, nor are qualitative techniques necessarily hermeneutic.(95) As such, pragmatists advocate integrating methods within a single study.(96) Moreover, Sieber (97) stated that because both approaches have inherent strengths and weaknesses, researchers should utilise the strengths of both techniques in order to understand better social phenomena. Indeed, pragmatists ascribe to the philosophy that it is the research question that should drive the method(s) used, believing that 'epistemological purity does not get research done'.(98) Bryman discusses how "this position with regard to the debate about quantitative and qualitative research prioritises the research question and relegates epistemological and ontological debates to the sidelines".(99) This stance is supported by Teddlie and Tashakkori (100) and Erzberger and Kelle. (101) In considering methods for this study, I have adopted a pragmatic philosophy and have allowed the research question to guide my choice of methods. A summary of the general characteristics and weaknesses of pragmatism are summarised in Table 3-1

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Table 3-1 Table summarising general characteristics and weaknesses of pragmatism⁽¹⁰²⁾

General characteristics of Pragmatism	Considerations
Finds a middle ground between philosophical dogmatism and scepticism and to find a workable solution	Basic research may receive less attention than applied research because applied research may appear to produce more immediate and practical results
Rejects traditional dualisms and generally prefers more moderate and common sense versions of philosophical dualisms based on how well they work in solving problems	Pragmatism may promote incremental change rather than more fundamental, structural, or revolutionary change in society
Knowledge is viewed as being both constructed and based on the reality of the world we experience and live in	Many come to pragmatism looking for a way to get around many traditional philosophical and ethical disputes. Many current philosophers have rejected pragmatism because of its logical failing as a solution to many philosophical disputes
Theories are viewed instrumentally (they become true and they are true to different degrees based on how well they currently work; workability is judged especially on the criteria of predictability and applicability)	
Prefers action to philosophising and offers the "pragmatic method" for solving traditional philosophical dualisms as well as for making methodological choices	

3.3 Use of the MRC guidance for this project

The original MRC framework published in 2000 (28) characterised the process of development through to implementation of a complex intervention in terms of the phases of drug development

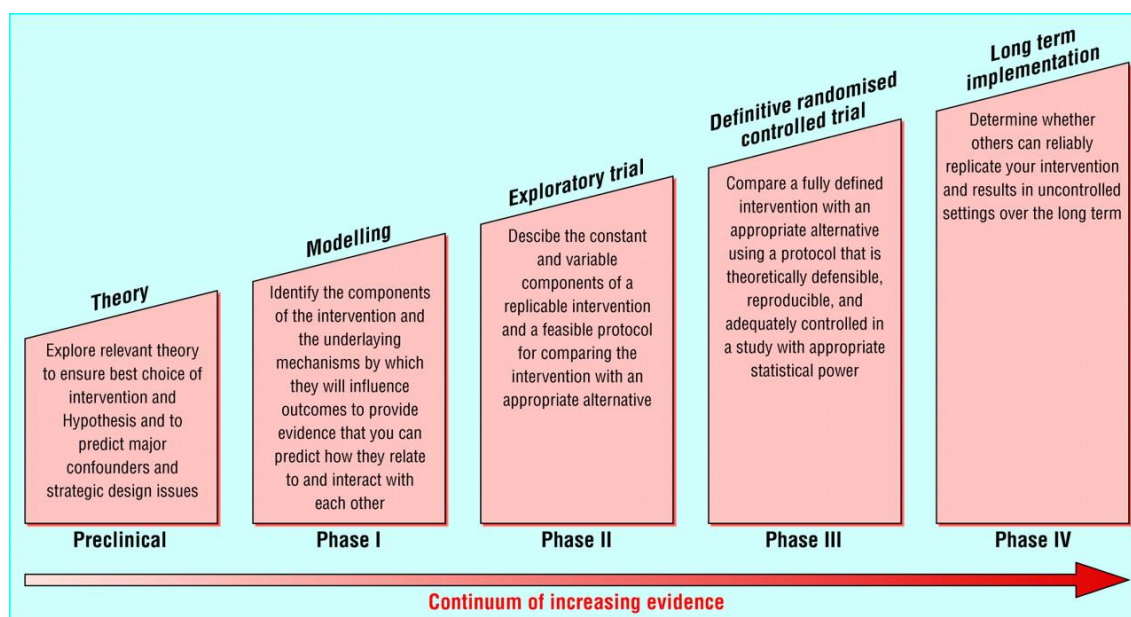


Figure 3-1 Sequential phases of developing randomised controlled trial of complex interventions as shown in the MRC framework 2000 (103)

However, in practice these may not follow a linear or even a cyclical sequence.(104) Craig et al (105) discuss how several authors have identified limitations in the 2000 framework and recommending, for example, greater attention to early phase piloting and development work (106), a less linear model of evaluation process (104), integration of process and outcome evaluation (107), recognition that complex interventions may work best if they are tailored to local contexts rather than completely standardised (108) and greater use of the insights provided by the theory of complex adaptive systems.(109) Subsequently, the MRC framework was subsequently updated from that shown in Figure 3-1 Page 107 to that shown in Figure 1-4 Page 24.

In developing and evaluating the H2H CC for the PIF-ILD population, the **Development** and **Feasibility and Piloting** stages of the MRC guidance have been undertaken. The MRC guidance advises researchers to select a study design most suited to the intervention with particular consideration given to the choice of outcomes. In addition, the guidance recommends the use of a wide range of study designs. I have therefore used a systematic review, qualitative

methods and quantitative methods within a randomised controlled trial. How each individual study fits into the MRC guidance is shown in Figure 3-2 Page 108.

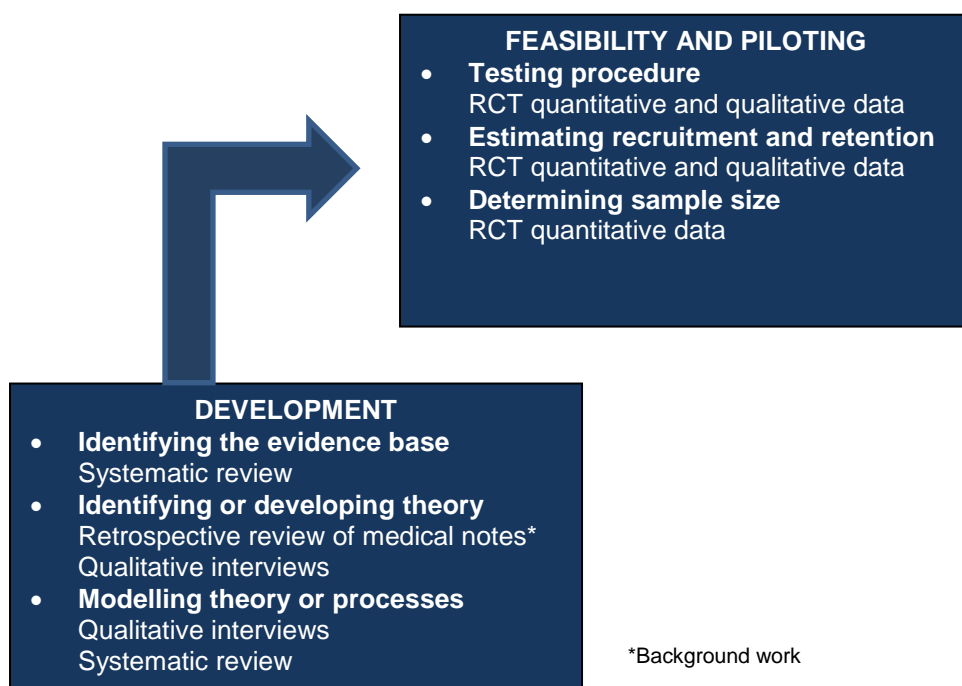


Figure 3-2 Use of the MRC guidance in developing and evaluating H2H for PIF-ILD

This body of work will consist of an initial **Development** stage followed by the **Feasibility and Piloting** stage. Findings from the **Feasibility and Piloting** work will be used to inform future **Development** and **Evaluation** work as appropriate. However, this will not form part of this thesis.

Three shortcomings for the MRC 2008 guidance were identified by the MOREcare group(14): a)moving from **Feasibility and Piloting** to implementation without robust evaluation; b) failing to develop the feasibility of the evaluation methods alongside the feasibility of treatment/intervention; and c) lack of theoretical framework underpinning treatment/intervention. A key point in the MOREcare recommendations (14) was that considerations about implementation be integrated into all phases of evaluation rather than only at the end. This is represented in the diagram in Figure 3-3 Page 109.

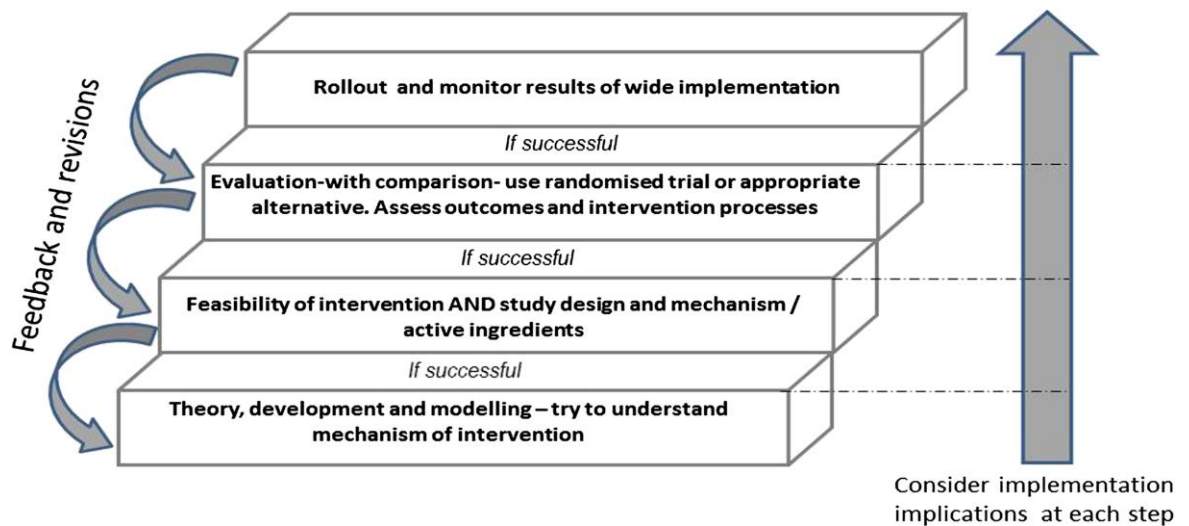


Figure 3-3 Key steps in developing and evaluating EoLC interventions in MOREcare guidance (14)

I will aim to address each of these issues during this study whilst ensuring that I am closely following the MOREcare recommendations (Table 1-1 Page 26) within the MRC guidance.

3.4 The use of mixed methods

The methods for this study are determined by the aims. In developing a complex intervention, mixed methods are needed. The MRC guidance (13) and MOREcare statement (14) both recommend the use of mixed methods. Mixed methods studies have become increasingly common in health services research.(110) It is recognised that mixed methods are more time consuming and expensive with the researcher having to learn new skills to be able to conduct mixed methods research to a high standard.(102) However, the advantages are felt to outweigh the disadvantages in this case. Justification for their use is shown in Table 3-2 Page 110.

Table 3-2 Table to show possible reasons for mixing methods.(111, 112)

Offset	refers to the suggestion that the research methods associated with both quantitative and qualitative research have their own strengths and weaknesses so that combining them allows the researcher to offset their weaknesses to draw on the strengths of both.
Completeness	refers to the notion that the researcher can bring together a more comprehensive account of the area of inquiry in which he or she is interested if both quantitative and qualitative research are employed
Unexpected results	refers to the suggestion that quantitative and qualitative research can be fruitfully combined when one generates surprising results that can be understood by employing the other.
Credibility	refers to the suggestion that employing both approaches enhances the integrity of findings.
Triangulation	seeks convergence, corroboration, and correspondence of results from the different methods.
Complementarity	seeks elaboration, enhancement, illustration, and clarification of the results from one method with the results from the other method
Development	seeks to use the results from one method to help develop or inform the other method
Initiation	seeks the discovery of paradox and contradiction, new perspectives of frameworks, the recasting of questions or results from one method with questions or results from the other method.
Expansion	seeks to extend the breadth and range of inquiry by using different methods for different inquiry components.

The MRC guidance and MOREcare statement state that mixed methods can be appropriate in all phases of development and evaluation. The MOREcare statement gives specific checklists for ensuring that mixed methods are used appropriately when designing and evaluating complex interventions in EoLC research (please see Table 1-1 page 26). This will be followed and referenced where appropriate.

I believe there is a place for the use of mixed methods in palliative care and more specifically PIF-ILD research where the complex end of life experience may not necessarily be fully captured in the quantitative nor the qualitative methods alone. Lindell et al(113) conducted a mixed methods RCT of 21 patients looking at a disease management program delivered using a format of support group for both IPF patients and informal caregivers with a control group of best usual care. They found that on quantitative analysis, there was increased anxiety and decreased QoL in the intervention group. However, the qualitative work showed that patients did

not feel isolated and felt the intervention had enabled them to put the disease into perspective, gave comfort and provided an improved mental picture. In this instance, the use of mixed methods allowed the authors to identify important discrepancies and identify inconsistencies between results found from the two different methods.

3.5 Rationale for mixed methods as applied to this study

The MRC guidance and MOREcare statement state that mixed methods can be appropriate in all phases of development and evaluation of a complex intervention. The MOREcare statement gives specific checklists for ensuring that mixed methods are used appropriately when designing and evaluating complex interventions in EoLC research (please see Table 1-1 page 26). This will be followed and referenced where appropriate.

The MOREcare guidance(14) recommends that the theoretical paradigm and method of integrating results should be defined at the outset:

In deciding on the model of the mixed methods design in this study, two main questions needed to be addressed(102):

1. Which research paradigm was to take prominence or was dominant?
2. In what order should the qualitative and quantitative components come?

For this study the initial **Development** phase of the study was represented by a smaller qualitative component which informed the larger quantitative component in the **Feasibility and Piloting** stage. A smaller component of qualitative interviews in the **Feasibility and Piloting** stage was also conducted to complement the larger quantitative data.

3.5.1 Qualitative component

In order to develop a complex palliative care intervention for patients with PIF-ILD it was first important to explore in detail the patients' and informal caregivers' needs and experiences of the disease. In doing so, a qualitative approach was used. Qualitative methods have been shown to provide a richness of data, with emergent theories and allow the researcher to delve deeply into issues.(41) In using qualitative methods, I aimed to explore in detail the specialist

palliative care needs of these patients and informal caregivers. This then allowed me to assess the full impact of the disease and allowed me to optimise the intervention in line with the perceived needs of patients and informal caregivers triangulated with HPs' views. Through conducting these interviews, I also aimed to maximise the cultural and local appropriateness of the adapted H2H intervention as recommended by the MRC guidance (13) and the MOREcare guidance (14). Interviewing HPs at this stage ensured that the intervention was understood by some key HPs and it may have helped to gear up potential stakeholders for this model of care, helping with recruitment for the **Feasibility and Piloting** phase. These interviews also informed appropriate outcomes for evaluating the intervention as part of the *modelling process and outcomes* stage of the MRC guidance (13).

Qualitative interviews were used in the **Feasibility and Piloting** stage to firstly assess the effects of implementation which may not have been measured by the quantitative outcome measures improving both internal and external validity. This ensured that the quantitative data collected through the outcome measures was placed in the context of the experiences and views of the patients, informal caregivers and HPs. The qualitative interviews reinforced what was found during the quantitative data analysis but also explained any unexpected findings. Secondly, to assess acceptability. Qualitative interviews were conducted of patients, informal caregivers and HPs to assess views of the H2H intervention and whether the needs of patients and informal caregivers were met during the intervention. The MOREcare guidance (14) recommends including patients' experience of care as an outcome and I aimed to examine this through the qualitative interviews. Finally to inform a future **Evaluation** trial. The interviews were used to examine any barriers to recruitment and retention. Questionnaire burden was also assessed.

3.5.2 Quantitative component

Quantitative outcome scales were used in the **Feasibility and Piloting** trial. The quantitative measures used in the **Feasibility and Piloting** trial were important to provide measureable information on acceptability, feasibility and possible effects of the adapted H2H intervention which may be used alongside the qualitative work to begin to further develop the intervention in

the *modelling process and outcomes* stage or to provide information for a future **Evaluation** or phase III trial.

The systematic review I conducted looking at interventions to improve symptoms and QoI in PIF-ILD included 35 studies. Only one study, authored by Lindell et al (113), used qualitative methods. Study results from the **Feasibility and Piloting** stage should be interpreted cautiously as effects may be smaller or more variable and response rates lower when the intervention is rolled out across a wider setting.(105) However, a preliminary positive result on quantitative outcome measures in the **Feasibility and Piloting** stage may be promising and warrant further examination in a full **Evaluation** trial when the intervention may then be compared to the other interventions from the review.

3.6 Integration and the added value of the various components in the larger mixed methods project.

For this study the initial **Development** phase of the study is represented by a smaller qualitative component which informed the larger quantitative component in the **Feasibility and Piloting** stage. A smaller component of qualitative interviews in the **Feasibility and Piloting** stage was also conducted to complement the larger quantitative data. Diagrammatic representations of methods, showing the sequential nature of the qualitative and quantitative methods, how the various components of the research will fit together and their application to the MRC guidance are depicted in Figure 3-4 Page 114.

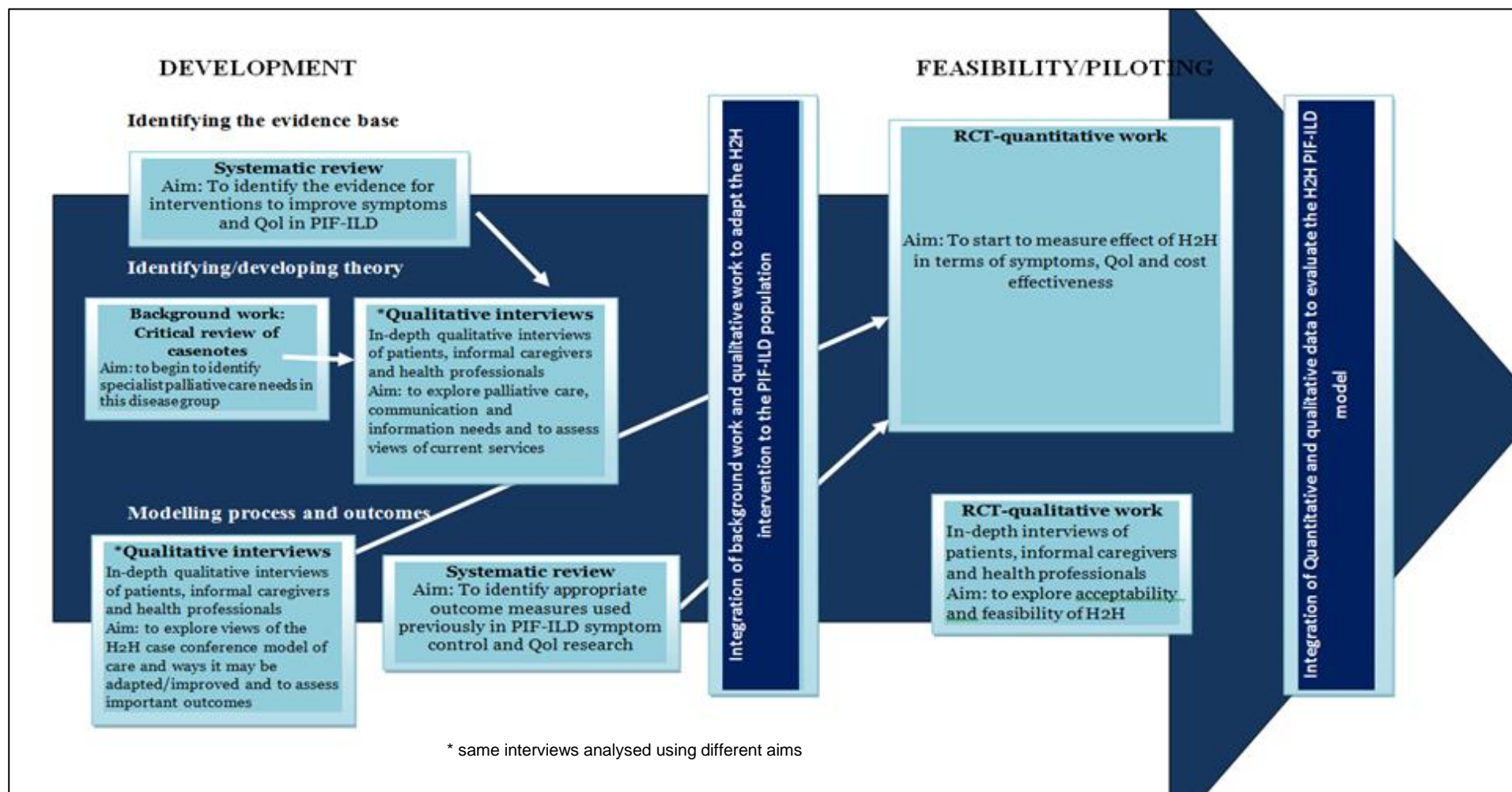


Figure 3-4 Diagrammatic representations of methods showing the sequential nature of the qualitative and quantitative methods, how the various components of the research will fit together and their application to the MRC guidance: size of qualitative and quantitative boxes reflective of prominence of research paradigm in MRC guidance

3.7 Ethical approvals and considerations

3.7.1 Ethical approvals

The qualitative phase of the project received initial approval from the Research Ethics Committee through addition as an amendment to a project already being conducted at King's College Hospital and Royal Brompton Hospital on the same group of patients (South West London REC 4, reference number 09/H0806/74 AM02). Approval for the RCT and qualitative interviews for Phase II was granted by the NRES Committee London – Chelsea (reference number 11/LO/0999). Site-specific approval was received from the Research and Development departments of King's College Hospital, Royal Brompton Hospital and St. Christopher's Hospice. An amendment for change in QoL outcome measure was approved (ref number AM1205/48). A second amendment for change in wording on information sheets and inclusion criteria was also approved (ref number 2 21.08.12). Ethics application, amendments and approvals are included in APPENDIX A.

3.7.2 Ethical considerations

The ethical issues raised by palliative care research are, for the most part, not unique to this field.(114) However, they are often magnified in this group. These include the vulnerability of the population, high rates of mental capacity and emotional distress at the end of life creating challenges to informed consent, addressing conflicts of interest within the dual roles of the clinician-researcher, the invasiveness and increased frequency of testing relative to standard clinical practice, and questions of scientific value that must balance the benefits and burdens of the intervention.(115) I will discuss each of these issues and their relevance to PIF-ILD and this study:

- Informed consent

People at the end of life, as at every other stage of life, deserve the best possible care. It has been the central focus of the palliative care movement, through research, education and practice, to reach this standard. The involvement of people near to death in this research ensures that their problems are illuminated and the most effective solutions are developed. PIF-

ILD patients are a group in which very little palliative care research has been conducted and as a result there is very little recognition of their palliative care needs. Subsequently, they are receiving sub-optimal care. PIF-ILD patients as part of wider group of vulnerable palliative care patients warrant additional scrutiny to ensure informed consent is obtained. However, informed consent deserves close scrutiny in all clinical research.(114).

Therapeutic misconception is a further threat to decision-making capacity in participants in end of life care research. This refers to the situation that occurs when a research subject fails to appreciate the distinction between clinical research and ordinary treatment, and may inaccurately attribute therapeutic intent to research procedures.(116) This may be a realistic outcome, if a new intervention is under study, but may represent a form of therapeutic misconception, where there is ambiguity about the goals of research. There is a clear need to be explicit about the goals of research and realistic about the benefits of participation during the consent process, especially when personal benefit may be a significant motivation for participation. In this study it was made clear when obtaining consent that the H2H intervention was in the preliminary stages of being tested and that it may improve symptom control and quality of life but that there was no evidence currently that it did.

Undue influence refers to a situation in which the influence of a caregiver or institution, knowingly or otherwise, leads to an individual to change his/her decision to participate in research affecting his voluntariness. There is evidence that doctors have a significant influence on their patients' decisions to participate in research at the end of life. In a survey of 101 patients in an Australian oncology centre, 84% of patients were very likely to participate in research if their doctor was keen.(117) Debt of gratitude to care providers or institutions may also be an additional motivator of patients' willingness to participate in research.(118) These concerns about professionals compromising a participant's voluntariness are not unique to end of life care research, operating wherever individuals are dependent on care providers, invest great trust and/or or have a debt of gratitude towards them. The ultimate safeguard against coercion and undue influence in theory involves maintaining independence of care providers and research wherever possible. For one year of recruitment of the RCT, I was working clinically at the Royal Brompton Hospital. If an inpatient was suitable for enrollment into the trial, I would ask the H2H CNS to approach the patient. If this was not possible, another member of the clinical team (who was not a member of the research team) would approach the patient to

initially discuss the study. When obtaining consent for the study, it was made clear to the patient and informal caregiver (both verbally and in the consent form) that if they did not wish to take part in the study, this would not affect their clinical care.

The need for continuing consent also raises ethical concerns in longitudinal studies.(119) In this study, the RCT raised concerns as the participants' consent was not retaken after entry into the study. However, participants could choose not to return the questionnaires if they no longer wished to take part and they could withdraw from the study at any time if they so wished. In addition, if the patient lost capacity, they were no longer asked to continue taking part in the study. As recommended by the MOREcare guidance, I have worked within legal frameworks on mental capacity.

- Recruitment and retention

Interventional studies, including RCTs, are generally considered higher risk in their potential burden than descriptive research. Where there is equipoise to justify a RCT, it is accepted that the risk of harm to the subject in being randomised to receive the inferior treatment is justified by the chance of benefit in receiving the superior treatment. However, this becomes difficult to justify in palliative care patients. To try to balance this, I adopted the fast-track design for the RCT to allow all participants to receive the intervention. This was also thought to have the advantage of being able to improve recruitment rates. To further improve recruitment, I followed the guidance as recommended by Jordhoy et al (120) which included firstly using several recruitment techniques (giving thorough and repeated personal information to the referral units, monitoring all inpatient and outpatient units, co-operating and developing good relationships with HPs in ILD services), I monitored the recruitment rates and changed or improved techniques as needed, I used simple phone call/email referral routes that imposed minimal workload on busy ILD colleagues and I allowed for attrition in the sample size calculation for the RCT.

Retention of patients in palliative care studies is difficult (121) as the majority of attrition is due to advancing disease or death. As directed by the MOREcare research method guidance on statistical issues (121), to improve attrition, meaningful timing of end points for the RCT were calculated which would allow minimal attrition whilst providing primary outcome data. In

addition, for the RCT, informal caregivers were still able to take part in the study and complete outcome measures if the patient became too unwell to do so.

- Concerns about risks, potential benefits and burdens

A recent systematic review of palliative care oncology literature identified that 66% of studies were non-therapeutic in nature.(122) However, it is possible that interviews and surveys may still incur risk at the end of life where there is emotional or physical distress.(123) It is recommended that interviews of patients near the end of life should employ mechanisms to assess and manage distress if it occurs. (114) Therefore, the interview length in this study was a maximum of 45 minutes. The interviews were organised at a time and location convenient to the patient and could be stopped at any time if they were not keen to proceed. Any interview could be split into two parts over two consecutive days if the participants preferred. After any interview, adequate time was allowed to check the impact and effect of the interview on the interviewee. Interviewees were also directed to the appropriate source of health/social care professional as necessary and were provided with relevant information about local counselling services, and with the interviewee's consent inform their GP/community medical teams of any concerns. If there was a high level of concern about the participant after the interview, this was urgently discussed with the principle investigator and the clinical team, to decide the most appropriate course of action.

It has been noted that it is not necessary that researchers need to inform participants that they are “near the end of life”, either in the consent process or throughout data collection as this may cause distress in itself.(114) The information sheets provided to the patients in the RCT described their disease as “advanced fibrotic interstitial lung disease” but did not describe them as end of life. It was also noted that patients may not wish to discuss end of life planning issues and that this may cause distress if this was pursued. Therefore, at the baseline interview, the patients' and informal caregivers' information needs were assessed and if the patient or informal caregiver did not wish to discuss prognosis or end of life/advance planning at the H2H CC, this was done separately between the HP (with the patient's consent). All concerns of this nature were documented in the clinical record file for the patient or informal caregiver. It is apparent that participants in research at the end of life may derive great benefit from the experience of

participation, even in non-therapeutic research. Nonetheless risks must be minimised and justified and involvement of service users and experienced researchers in the design and implementation phases of research may be useful in this achieving this aim.(123) As directed by the MOREcare guidance(14), I collaborated with a patient and informal caregiver in the design of the study, vocabulary used in explaining the study and consent procedures. A patient and informal caregiver were part of the project advisory group available to give advice as needed.

It is recognised that in end of life care, research staff can experience similar 'burn out' to clinical staff, and the stress of interviewing terminally ill patients, observing their decline and eventual death builds up over time. Therefore, monthly team meetings were scheduled so staff could reflect and share concerns. There was also additional support if needed.

Evidence-based medicine, founded on research, has led to improvements in quality of patient care.(124) Importantly, there is a paucity of evidence to direct the delivery of palliative care to PIF-ILD patients. PIF-ILD patients should not be denied the opportunity to participate in research if they so wish and the research is ethically sound especially if this will mean that there is an improvement in the delivery of care for future patients. The MOREcare guidance (14) recognises that it is ethically desirable for patients and families in EoLC to be offered involvement in research. Throughout this study I have had an awareness of the ethical issues which may relate to patients, informal caregivers and staff and I have attempted to address these issues to the best of my ability.

3.8 Conclusion

In this chapter I have presented the overall methods for this study. I have shown in detail how I will use the MRC guidance alongside the MOREcare guidance to develop and evaluate the H2H model of care. Within this, I will use mixed methods. I have shown how I will integrate both research paradigms and I have defined the method of integration that will be used within each part of the study. Finally, I have considered the ethical considerations which are pertinent to this study.

I will now go onto present the qualitative work which will form part of the *identifying/developing theory* and subsequently the *modelling processes and outcomes* part of the MRC guidance.

Chapter 4 Qualitative work to assess the palliative care needs of patients and informal caregivers living with PIF-ILD

4.1 Introduction

In this chapter, the aims and methods of the qualitative work will be presented. Following this, firstly the results of the qualitative work used to build on the evidence base for the palliative care needs of patients with PIF-ILD will be presented. This will build on the evidence base of the palliative care needs of these patients and informal caregivers presented in Chapter 1 forming part of the *identifying theory/developing theory* stage of the **Development** Phase of the MRC guidance. Secondly, the results of the qualitative work forming the *modelling theory/processes* phase will be presented. Thirdly, the discussion of all the qualitative work will be presented. Finally a summary of the findings for the *modelling theory/processes* phase will be presented and integration of the results from the systematic review, retrospective review of case notes and qualitative work will occur to present the adapted H2H model of care.

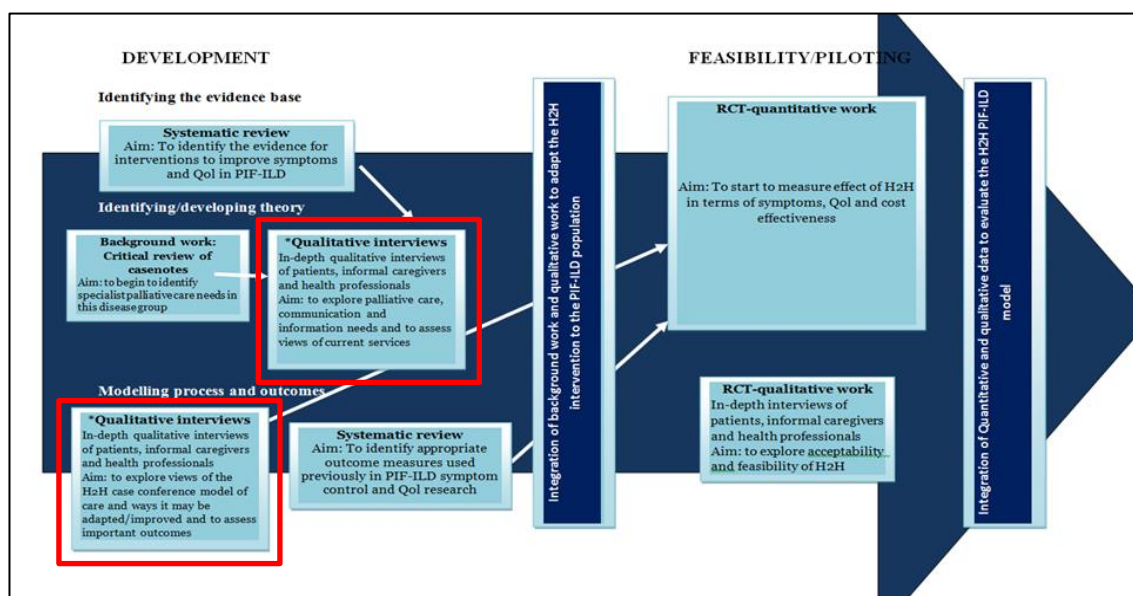


Figure 4-1 Figure showing qualitative work to be presented in overall plan of study

4.2 Aims of qualitative interviews

4.2.1 Identifying/developing theory phase

- To identify and describe specialist palliative care needs within this population.

4.2.2 Modelling processes and outcomes phase

- To identify patients', informal caregivers' and HPs' perceptions on co-ordination of care, communication and information needs.
- To explore patients', informal caregivers' and HP' views on the H2H model of care and ways in which it may be improved/adapted for the PIF-ILD population.

4.3 Methods of qualitative in-depth interviews for Development

Phase

4.3.1 Settings and Participants

Interviews took place between December 2010 and March 2011. Patients and informal caregivers were recruited from the Royal Brompton and Kings College Hospital NHS Foundation Trusts. The Royal Brompton Hospital (RBH) is a specialist ILD centre in central London. The unit has one of the largest diffuse lung disease patient populations in the world with over 500 new referrals a year for patients with ILD from across London and the surrounding counties. Patients come from areas with varying palliative care services and community support teams. King's College Hospital (KCH) is a tertiary hospital with a specialist ILD clinic in the south-east of London. KCH serves a geographical area characterised by material and social deprivation in addition to a large population of black and minority ethnic communities. The area has a network of palliative care services including inpatient hospices, community services and hospital support teams, co-ordinated through the South London Palliative Care Network and other regionally based networks.

Patients with PIF-ILD and TLCO (percentage predicted transfer factor) <40%, informal caregivers of patients with PIF-ILD and TLCO <40% and HPs involved in the care of these patients were invited to participate in the study. HPs were recruited from RBH, St Christopher's Hospice and primary care. St Christopher's Hospice is part of the St Christopher's palliative care services which deliver palliative care in a range of settings including patients' homes, in-patient wards and a day centre. It serves a diverse population of 1.5 million people in the London boroughs of Bromley, Croydon, Lambeth, Lewisham and Southwark, reaching some of England's most deprived areas.(125)

Other study inclusion criteria included an ability to understand and speak English fluently. Those under 18 years of age, with cognitive impairment or those unable to provide informed consent were excluded.

Participants for the whole study were selected purposively. This is a process whereby particular participant characteristics are purposively sought out and sampled. Gysels and Higginson(126) describe this form of sampling which allows a:

'case orientated approach in qualitative research as opposed to variable orientated in quantitative research.....[allowing] balancing of the richness of the data with the relative representativeness of the sample'.

Qualitative sampling strategies are not designed to achieve statistical generalisation or test hypotheses. Instead qualitative research takes an inductive approach and involves the in-depth study of the range and complexity of meanings and phenomena relevant to the research question with the aim of providing explanations and conceptual generalisation. (127) A purposive sampling frame was therefore devised to include potential patient participants of different age ranges (< or > 70 years), from different ethnic backgrounds, with or without respiratory or cardiovascular co-morbidities, with or without community palliative care input, and with or without informal caregiver support. The rationale for this was to ensure fair representation of different groups of patients required to address the study aims. For informal caregivers, inclusion criteria included that they were caring for someone who met the patient inclusion criteria and they had an ability to understand and speak English fluently. Those under 18 years of age, with cognitive impairment or those unable to provide informed consent were excluded. For HPs, a wide range of multi-disciplinary HPs managing the care of ILD patients meeting this criteria were sought from both the primary and secondary care setting.

I attended ILD clinics at both RBH and KCH and discussed potential participants with members of staff involved in their care to identify whether participants met inclusion criteria. Potential participants were then invited by the clinical teams to participate in the research, and if they agreed, were then approached by myself for further discussions about the study and to address any questions or concerns they had. Informal caregivers were identified by patients and HPs. Potential HP participants were identified by patients, informal caregivers already participating in the study and other HPs.

It was made clear that I was part of the research team rather than the clinical team. Where possible, I did not reveal that I was a doctor nor that I was from a palliative care background. Despite clear explanations about the 'research' role being distinct from the 'doctor' role, I felt that this was bound to have some impact on the interview and type of information offered by the interviewees.(128) For instance, if the patient or informal caregiver had experienced poor service provision from a member of the medical staff, I did not want information to be withheld because the participant was concerned that they may offend me. I wished to reflect a naïve

curiosity to the participant which would not influence their response and allow me to obtain the richest unbiased data as possible.

4.3.2 **Consent**

I approached the participants to give the information sheets and discuss the study. Where possible, a quiet environment was sought to do this. However, this was not always possible and at times these conversations were held in a busy clinic waiting room. There did not appear to be any difference in the questions that were asked or refusal to participate when this occurred. I answered any questions that participants had before obtaining informed consent. Two interviews were conducted at a later date at the participants' request. Where possible, participants were interviewed on their own to ensure that there was minimal bias. This was possible for all but one interview (Mary, whose daughter was present).

HPs were identified by the clinical teams and I contacted them via email when I also sent the information sheet. HPs were interviewed in their normal place of work at a time convenient to them. All participants underwent interview in the setting of their choice. Informed consent was obtained prior to starting the interview. Whilst obtaining informed consent and prior to starting the interview, participants were assured that they could request for the interview to be stopped at any stage and for any reason.

The interview process began by introducing the research and who I was. It was made clear that all data would be anonymised and kept completely confidential to anyone outside the research team. It was explained that the interview would be audio recorded and that if there were any questions that the participant did not wish to answer, then they could choose to omit or terminate the interview. In addition, it was explained that if the participant required a break or had any questions which they did not wish to be part of the interview, then the tape could be stopped.

Recordings were made using a small unobtrusive digital recorder which was placed between myself and the participant. No one objected to the interview being recorded nor did anyone ask for the recording to be stopped during the interview. A few of the participants did appear nervous and whether this was due to the interview being recorded was unclear. However, all participants appeared to relax once the interview was underway.

4.3.3 Topic guide

The interview broadly followed the topic guide shown in Table 4-1 Page 125. This was developed based on the literature and discussion with experts on the Project Advisory Group. The interviews were semi-structured so even though the topic guide provided direction and highlighted areas that needed to be addressed, I was initially led by the participant in the path that the interview took.

Table 4-1 Topic guide for qualitative interviews

Patient	Carer	HP	Prompts
How does your disease affect you?	How does the disease affect your loved one?	How does the disease affect patients and carers?	Physically (symptoms and what helps relieve), psychologically, socially (Activities of Daily Living - ADLs, personal/relationship issues)
What things are most important for you about your disease?	What things are most important for your loved one about the disease?	What things are most important for patients and carers about the disease?	
What do you feel are the most important things that affect your QoL?	What do you feel are the most important things that affect your loved ones QoL?	What do you feel are the most important things that affect patients and carers QoL?	
What is your understanding of your disease and how do you see your illness progressing in the future? Have you made any decisions about your treatment and care when you are less well?	What is your loved ones understanding of their disease and how do they see their illness progressing in the future? Have they made any decisions about treatment and care when they are less well?	What do you think patients understand about their disease and the future? Have they usually made decisions about treatment and care when they are less well?	
Who is currently involved in helping with care?	Who is currently involved in helping with care?	Who is usually involved in delivering care to the patient?	Who helps with ADLs, physiotherapist, respiratory nurse, community palliative care team, district nurse, GP
Would you like more help with anything in particular? What?	Would you like more help with anything in particular? What?		
What do you think about current services available to you?	What do you think about current services available to your loved one?	What do you think about current services available to ILD patients?	Prompts: What do you think about current symptom management, hospital care, community care, CC model of care, communication between the two, information provided to you about the disease, planning for when less well/ end of life?

The interview began with a general exploration of how the disease affected the participant. Probing and possibly difficult questions about end of life planning were left till the middle of the interview to allow participants to relax and become accustomed to the interview surroundings and the interviewer. All issues were explored in detail with both verbal and non-verbal cues followed up. I made field notes during and after the interview where appropriate. This allowed me to note reflections. Participants were warned that the interview was coming to an end to allow them to discuss any issues they felt necessary. I concluded the interview with less probing and upsetting questions about service provision.

At the end of the interview, participants were asked if they felt there was anything that had been missed or anything they would like to add further information to and were again assured of confidentiality.

I had not previously conducted qualitative interviews. In preparation, I did extensive reading and practice interviews with colleagues (Tom Osbourne and Fliss Murtagh) within the department and my family members who provided constructive feedback. I also sat in as an observer on interviews conducted by an experienced qualitative researcher within the department. During this time, I learnt the importance of the spoken and non-spoken word. I refined my skills on picking up verbal and non-verbal cues and following them up appropriately with the use of silences or gentle probing. I discussed and made a plan of how I may handle upset participants with supervisor IJH. This allowed me to gain confidence in an area that I had no previous experience. Practice interviews conducted by myself were transcribed and reviewed by supervisor IJH to provide feedback on transcribing technique, interview skills and content.

4.3.4 Conduct

I realised that the success of the research was dependent on my being able to form relationships with the participants, especially patients and informal caregivers as these were the participants that I hoped to elicit sensitive information from. This involved me gaining their confidence and trust which necessitated some emotional input on my part in the relationships (129) and awareness on my part of the emotional, practical and physical needs of the participants. However, I was also aware of the feelings and responses which I had in the interview and what I portrayed to the interviewee.(129) I felt it important to strike the right

balance between empathy and influencing the direction in which the interview would continue. I conducted interviews away from the outpatient department where possible to facilitate this. This was balanced with the fact that patients became symptomatic when moved to another location. If this happened, the patient would be given as much time as needed to recover and become comfortable before the interview was commenced. Care was taken to ensure that participants were comfortable during the interview process. In addition, I was aware of the clothes that I wore. Smart (130) in conducting her research 'definitely experienced dress as a subtle but important aspect of doing the research'. Taking this into account, I aimed to dress in suitable attire to reflect respect for the interviewees but not so smart that I may be imposing and unapproachable.

I often had to wait for long periods in the outpatient department awaiting referral of appropriate patients. At times I felt uncomfortable as I was worried that I may be a nuisance. Where possible, I tried to develop relationships with the clinical staff to facilitate referral. However, I did sometimes feel that the medical staff were resentful that I was not helping in the busy clinics or giving palliative care advice where needed.

There were a wide range of emotions expressed during the interviews and at times both the patients and informal caregivers became upset. In certain instances, it was difficult to continue to probe when participants were upset. I found silences very helpful and productive in allowing participants to collect themselves and then continue without interruption. I used my experiences as a palliative care doctor and courses attended in communication skills to handle sensitive issues. I used gentle prompts where silences were not helpful. Where possible I refrained from counselling participants during the interview if they became upset. However when the interview was over, I would always readdress any issues that had caused the participant to become upset, and offer advice or counselling if appropriate. I felt it ethically inappropriate to not do this. As I was doing this after the interview had been completed, I felt that it did not affect the information that I gathered. I believed it important to ensure there was overall non-maleficence from taking part in the interview process but I also recognised the importance of not biasing the data during the interview. I have completed a Masters degree in the Ethics of Cancer and Palliative Care and used skills that I learnt during this degree and during my clinical work to recognise and achieve this balance.

Some informal caregivers and patients did demonstrate a tendency to exhibit social desirability. For instance, informal caregivers would initially say that marital relationships were unaffected by the disease but on gentle and deeper probing, it became clear that this was not the case. All participants were older than I was with the majority of patients and informal caregivers 30-40 years older. It is possible that this was a factor in them wanting to exhibit social desirability. Nevertheless, I felt that interviewees opened up during the interview and overall these factors did not hamper the quality and depth of information obtained.

Participants appeared motivated to help take part in the interviews largely because they wanted to help research in an area they felt was under researched. In fact, certain participants demonstrated their interest and commitment by suggesting other participants that they believed would want to take part. A number of participants (including those who had become upset during the interview) expressed that they were glad that they had participated and they had found it to be a valuable experience.

Even though at times it was hard work and emotionally draining, I experienced a great deal of personal enjoyment from the sustained contact over time with these participants. I felt a genuine pleasure in learning of their disease experiences as well as feeling very privileged that participants felt able to 'open up to me' about intensely personal issues.

4.3.5 Data analysis

All interviews were digitally recorded and then transferred verbatim onto a secure transcription database at the Royal Marsden NHS Foundation Trust. Two palliative care secretaries (one with previous experience of qualitative interviews), who received appropriate training transcribed the 18 interviews verbatim. All interviews were anonymised during this process.

Multiple approaches exist for analysing qualitative data. For example, the use of qualitative analysis approaches such as thematic analysis and Framework analysis are suitable for researchers who wish to pragmatically employ a relatively low level of interpretation. In contrast, grounded theory and interpretative phenomenological analysis (IPA) attempt to achieve a higher levels of complexity demanded by the research question. (131) Appraising the different qualitative methods is a field in evolution. The inherent strengths and limitations of using different analysis methods considered are presented in Table 4-2 Page 130.

I adopted a constant comparison approach (132) facilitated by Framework analysis, as described by Ritchie and Spencer. (133) This provided me with clear steps to follow and finally produced highly structured outputs of summarised data. (134) The nature of Framework approach had intuitive appeal; it provided a clear, pragmatic and transparent structure for me, a first-time qualitative researcher.

Although the framework approach can appear to be mechanistic, it elegantly condensed participants' accounts that facilitated inspection of data across themes and cases. At the same time the analysis aimed to maintain as much closeness to the original data as possible, by adopting the participants' narrative as far as possible. Moreover, I also chose the framework approach as it allowed me to conduct both a deductive and inductive approach to analysis. In the deductive approach to the analysis, themes and codes were preselected based on previous literature, theories or the research question. The inductive approach permitted me to identify new emerging themes from the data, independent of the coding framework.(134)

Table 4-2 Table to compare different qualitative analysis methods ⁽¹³⁴⁻¹³⁷⁾

Method	Approach	Analysis	Pros	Cons
Thematic analysis To describe the content of text or communication objectively, systematically and quantitatively.	Process of data reduction. Uses categories, often derived from theoretical models. Manifest content analysis is the analysis of visible or apparent content e.g frequency of words	Identifies themes i.e. patterns found in the information that at the least describes and organises or at the most interprets aspects of the phenomenon. Descriptions of the data are derived, classified and coded into categories for analysis. A coding framework can serve to divide the data into quantifiable units.	Systematic and replicable technique for compressing many words of text into fewer content categories based on explicit rules of coding. It has the attractive features of being unobtrusive, and being useful in dealing with large volumes of data	Synonyms may be used therefore may lead to underestimation of importance of a concept. Different words may not represent a category equally well
Framework analysis Difference between framework analysis and thematic analysis is the final stage of looking at relationship between codes i.e mapping and interpretation for associations between codes	Geared towards generating policy and practice-orientated findings- developing practical strategies on basis of analysis	Familiarisation Thematic analysis Indexing Charting	Like grounded theory- integrity of individual respondent accounts is preserved throughout the analysis. Not aligned to any particular epistemological, philosophical, or theoretical approach- flexible for use in both inductive and deductive analysis	Easy to attempt to quantify qualitative data (eg 13 out of 20 participants said X)
Narrative analysis To reconstruct the interrelation of life events within the life world. Generates data in the form of biographical processes or stories	The narrative is seen as a true representation of the events recounted. The researcher as narrator provides an outline of individuals' stories, which the reader has to make sense of.	All non-narrative passages are eliminated first. The researcher then segments the text and refines the historical sequence of meaningful life experiences.	Accounts of participants which are "undistorted"	Imposing structure on a story
Grounded theory (also known as constant comparative approach) To develop a theory of the phenomenon in question which is more than a descriptive account. The aim is not to reduce complexity by breaking it down but to elaborate it by including context	Moves from descriptive classification of events and facts to an abstract theory that accounts for relationships and processes. The theory "emerges" from the data. The researcher must be alert to the influence of the field and not allow this to contaminate developing theory but rather to substantiate it.	Theory is developed from data which is then tested through further data collection and analysis. Constant comparative approach	Inductive and emergence theory without preconceptions Explains people's actions regardless of time and place.	Not a descriptive method

A number of stages were undertaken in the analysis process and these were familiarisation, identifying a thematic framework, indexing, charting and finally mapping and interpretation. These are described below:

4.3.5.1 Familiarisation

First, I listened to the tapes and re-read the interviews (with field notes) multiple times to immerse myself in the data and participants' stories about the disease. Even though I had conducted all the interviews and had gained an overall impression of the information that had been gathered, I felt this was important to set ideas and hunches into context and to ensure that recollections were not partial.(133) Moreover this process of immersing myself in the content of the interviews helped me to take stock and gain a feel for the material as a whole. In addition, this allowed the process of abstraction and conceptualisation to begin. Key ideas, recurrent themes, general atmosphere and difficulty of exploring particular subjects were noted.

4.3.5.2 Identifying a thematic framework and Indexing

I then set up a framework within which the data gathered could be sorted and sifted. This was done through development of a formal coding scheme which consisted of reading and re-reading interviews and making notes about themes that were emerging. The coding index or scheme helped me to make sense of and helped me organise all the data derived from the participant interviews. To some extent this process was also helped by drawing on *a priori* issues- those drawn from the original research objectives and the interview schedule. Themes were then sorted and grouped into sub-themes that captured participants' views. A thematic framework with coding system resulted which is shown in Figure 4-2 Page 133.

NVivo 9 was used to manage data and index the data according to the coding scheme. I attended a course at King's College London to help further develop and refine my skills in using this qualitative package. All the data was read and annotated according to the thematic framework. A non-exclusive approach was used as some of the data could be coded into more than one category therefore single passages often contained multiple themes and codes and were coded as such. This helped to highlight and identify relationships/associations within the data. In addition, this allowed each code to be accessed and for me to review patterns and

contexts in which they arose. This was then reviewed by an iterative process with reflection back to the transcripts. Sometimes data was recoded after review. Themes and sub-themes were critically discussed throughout the process with supervisors IJH and JK. In addition JK independently reviewed and coded two transcripts of data. These were then compared and discussed to ensure rigour.(138)

1. Physical
 - 1.1 Shortness of Breath
 - 1.2 Fatigue
 - 1.3 Cough
 - 1.4 Anorexia/weight loss
 - 1.5 Decreased mobility
2. Emotional
 - 2.1 Increased episodes of anger
 - 2.2 Frustration
 - 2.3 Depression
 - 2.4 Change in personality
 - 2.5 Anxiety
3. Social
 - 3.1 Difficulty with ADLs
 - 3.2 Loss of independence
 - 3.3 Change in personal relationships
 - 3.4 Family relationships
4. Spiritual
 - 4.1 Unmet spiritual needs
 - 4.2 Spiritual distress
5. Information and planning
 - 5.1 Understanding of disease
 - 5.2 Information needs
 - 5.3 How disease will progress in future
 - 5.4 End of life planning
6. Care and Support
 - 6.1 Support strategies
 - 6.2 HPs involved in current care
 - 6.3 Satisfaction with current care
 - 6.4 How current care could be improved
7. Communication and CC model
 - 7.1 Views of current communication
 - 7.2 Views of CC model

Figure 4-2 Thematic framework and coding system used in qualitative interviews in Development phase

4.3.5.3 Charting

This process involved abstraction and synthesis of the themes that emerged from the interview transcripts. Each passage of text which had been coded with a particular code was studied and a condensed summarised version was abstracted and entered into a relevant blank cell in a chart in Microsoft Word. Participant terms were used as much as possible. The aim was to fill each cell with a summary of the relevant data, keeping as closely as possible to the original data by condensing its meaning and using participant terminology where possible. This allowed for the ordering of data by grouping similar content together. The chart had headings based on themes and sub-themes developed during analysis. This allowed me to build up a bigger overall picture of the data by considering the range of experiences, meanings, attitudes and views for each issue or theme.

4.3.5.4 Mapping and Interpretation

Mapping and interpretation of the data involved reviewing the charts and research notes. This allowed me to compare and contrast the perceptions, accounts/experiences and then search for patterns/connections and seek explanations for these internally within the data. In addition I aimed to understand and explain potential findings and discordant results where found. I discussed findings with my research supervisor (JK) reaching consensus on many issues. This iterative process enhanced the rigour of analysis and interpretation of the data and also allowed me to remain reflexive, to question findings and open to different viewpoints.

4.3.5.5 Rigour and validity

There has been debate that the inflexibility and confines of rigour and validity can threaten the very essence of qualitative research.(139) However, testing of rigour and validity are imperative to try to prevent researchers inventing results which may vaguely resemble but not authentically represent the entity being studied.(140) Criteria in the concept of validity in qualitative research include reflexivity, criticality, authenticity and integrity.(141) I will now discuss these in detail:

4.3.5.5.1 Reflexivity

As all data was collected and analysed by myself, my own personal perspectives should be considered (142) and have been taken into account when analysing the data as it may introduce bias. This is essential as I considered what the interviewees said, interpreted this and then asked further questions as well as conducting analysis. My previous experiences of patients was largely in the cancer setting and I had had very limited contact with PIF-ILD patients prior to commencing this research. I was aware that PIF-ILD was a life-limiting group of diseases and I had awareness that there could possibly be some burdensome symptoms. However, I did not come to the research with any preconceived ideas of how extensive this was. In addition I have had first-hand experience of patients with non-malignant shortness of breath. My father died in 2009 with end-stage heart failure. During his disease he had periods of uncontrolled shortness of breath. I am aware from a pathophysiological and clinical point of view that heart failure is very different to ILD and I would hope that my own personal experiences did not influence the interviews in a negative way. I feel at times that it made me a more empathetic and understanding interviewer able to connect more with the participants and added to my research.

Other contextual elements, such as social desirability and age differences may have introduced bias by affecting how the interviewee's responded to my questions.(143) However, where possible I tried to move beyond accepting what appeared to be superficial answers and pick up on non-verbal cues to facilitate more probing discussion.

4.3.5.5.2 Criticality

Where possible I have tried to give a detailed account how I intend to appraise my research findings. In addition I have looked at more unusual views when they have been expressed (searching for negative cases) and why this data may have emerged and what it means.(142)

4.3.5.5.3 Integrity

Dodd and Davies (144) comment in their paper on rigour in qualitative research that ethics in qualitative research needs to be looked at contextually and flexibly. Ways in which I have attempted to do this are that I have ensured that consent forms are clear that participants can

refuse to answer any question they feel uncomfortable about, I have had access to independent ethical advice from experienced qualitative researchers during data collection and analysis should any unexpected incidents occur, participants have had access to independent counselling support if needed and the study was reviewed by an independent ethics committee. In addition I have used my own ethical skills to continuously appraise my conduct during the research process.

All data has been kept in a manner that complies with the data protection act and the methodological detail has been optimised to enable another researcher to repeat the study. In addition, the rationale behind the sampling strategy has been made clear.

All names of patients, informal caregivers and HPs have been anonymised to ensure confidentiality. Participant names have been changed to names which are culturally and age-appropriate to try to make accounts come alive and illustrate each participant as an individual. Direct quotes are used within the text to illustrate key findings and reflect the original data and experience.

4.3.5.5.4 Authenticity

Member checking and respondent validation enhances the authenticity of qualitative research as well as the credibility and criticality.(142) However, due to time constraints this was not possible. Sample interviews and generalised findings were however presented to members of the Project Advisory Group which contained HPs and a patient. This is known as 'proxy respondent validation' where community representatives, stakeholders and experts are consulted to help ensure that data is interpreted in a representative and balanced way.(145)

In addition, authenticity has been demonstrated by quoting sections of relevant narrative from the transcripts to provide a lucid and life-like representation of the participant's experience which would allow the reader to appreciate the depth of the experience and provide supporting data for the points I have made in the analysis.(142) In addition, the interview was conducted as semi-structured and participants were allowed to discuss issues that were important to them and not just the issues that I was interested in which has also been shown to improve authenticity.(142)

4.4 Results of qualitative interviews

4.4.1 Participant details

Eight patients (four from RBH and four from KCH), four informal caregivers (from RBH) and six HPs agreed to be interviewed. The HPs comprised a respiratory physiotherapist, ILD specialist nurse, ILD Consultant, Community Palliative Care CNS, Community Palliative Care Consultant and General Practitioner. Five patient participants were male, four were older than 70 years and four were white British (other ethnicities were one Asian, one Afro-Caribbean, one Cypriate and one South American). No patient participants had community palliative care involvement. Five patient participants had informal caregivers. No patient and informal caregiver dyads were interviewed. Four informal caregivers interviewed were all from RBH and all white British.

Twelve patients were approached and four declined to be interviewed. Two did not feel that they had the energy to be interviewed and two did not have the time and also did not feel they could return at a later date. This represents a response rate of 67% from the patient group. Five informal caregivers were approached and only one declined (he did not wish to leave his wife) representing a response rate of 80%. All HPs approached agreed to take part.

The informal caregiver sample mainly comprised caregivers in spousal relationships but also included one daughter. All interviews except for that of Mary (name has been changed to ensure confidentiality), whose daughter was present, were conducted alone. The informal caregivers and patients interviewed had no relationship to each other.

Table 4-3 Description of participant characteristics (all names have been changed to ensure confidentiality)

Name of participant	Gender	Age	Ethnicity	Diagnosis	TLCO %	Co-morbidities	Palliative care involvement	Informal Caregiver
Patients								
RBH1 Terry	Male	81	White British	IPF	38	No	No	No
RBH2 John	Male	63	Asian	IPF	35	No	No	No
RBH3 Jim	Male	77	White British	IPF	33	Yes- COPD	No	Yes
RBH4 Peter	Male	65	White British	IPF	39	No	No	Yes
KCH1 Mary	Female	75	White British	IPF	36	Yes-osteoporosis	No	Yes
KCH2 Ruth	Female	56	Black Carribean	IPF	35	No	No	Yes
KCH3 George	Male	74	Cypriate	IPF	31	No	No	No
KCH4 Lea	Female	57	South American	NSIP	30	Yes- Rheumatological disease	No	Yes
Informal Caregivers						Relationship to patient		
RBHC1 Penny	Female	63	White	Wife of James (advanced IPF)				
RBHC2 Jane	Female	41	White	Daughter of Anne (advanced IPF)				
RBHC3 Joan	Female	55	White	Wife of Paul (advanced IPF)				
RBHC4 Anthony	Male	63	White	Husband to Betty (advanced IPF)				
HP								
HP1	Female					ILD Physiotherapist		
HP2	Male					ILD CNS		
HP3	Male					ILD Consultant		
HP4	Female					Palliative Care Community CNS		
HP5	Male					Palliative Care Consultant (community)		
HP6	Male					GP		

4.4.2 Symptoms

The three main physical symptoms reported by patients during the qualitative interviews were shortness of breath, cough and difficulty sleeping. In addition, patients reported depression and anxiety as significant problems. This is illustrated in Table 4-4 Page 139.

Table 4-4 Symptoms reported in qualitative interviews in Development phase

Number of reported symptoms (patients reported more than one symptom)	Patients (n=8)
Shortness of breath	8
Cough	5
Difficulty sleeping	3
Fatigue	1
Depression	5
Anxiety	2
Other	2

Whilst one patient reported one symptom, the majority of patients interviewed reported four or more uncontrolled symptoms. This is illustrated in Table 4-5.

Table 4-5 Number of reported symptoms in qualitative interviews in Development phase

Number of reported symptoms	Patients (n=8)
0	0
1	1
2-3	3
4-5	4

4.4.3 **Presentation of the qualitative findings related to the *identifying/developing theory* phase.**

In this section I will present details of the experiences and needs of patients and informal caregivers with PIF-ILD. This will be supplemented with the HPs' perspectives. I will first present the published paper, followed by more detailed results from further analyses. Participants' views have been presented alongside each other regardless of whether they are patients, informal caregiver or HPs. This is to provide different perspectives on emerging themes. Finally, I will discuss what the findings from the qualitative results presented indicate would be needed from the adapted H2H intervention.

Findings from the qualitative interviews and same data set related to end of life information needs and planning, which includes satisfaction with current care and views of the CC model of care, will be presented later in the chapter in a separate published paper.

4.4.3.1 **Bajwah S, Koffman J, Higginson IJ, Ross JR, Wells AU, Birring SS, Riley J. The palliative care needs for fibrotic interstitial lung disease: A qualitative study of patients, informal caregivers and health professionals. *Palliative Medicine* 2013;27(9):869-876**

The palliative care needs for fibrotic interstitial lung disease: A qualitative study of patients, informal caregivers and health professionals

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Abstract

Background: While there have been some studies looking at the impact on quality of life of patients with idiopathic pulmonary fibrosis, to date no qualitative research looking at the specialist palliative needs of these patients has been conducted.

Aim: This study aims to explore the specialist palliative care needs of people living with end-stage progressive idiopathic fibrotic interstitial lung disease.

Design and settings/participants: In total, 18 qualitative semi-structured in-depth interviews were conducted with patients, their informal caregivers and health professionals across two specialist interstitial lung disease centres in London and in the community.

Results: Many participants reported uncontrolled symptoms of shortness of breath, cough and insomnia, which profoundly impacted every part of patients' and informal caregivers' lives. Psychologically, patients were frustrated and angry at the way in which their illness severely limited their ability to engage in activities of daily living and compromised their independence. Furthermore, both patients and informal caregivers also reported that the disease seriously affected family relationships where strain was pronounced. There was varied knowledge and confidence among health professionals in managing symptoms, and psychosocial needs were often underestimated.

Conclusion: This study is the first of its kind to examine in depth the impact of symptoms and psychosocial needs revealing the profound effect on every aspect of progressive idiopathic fibrotic interstitial lung disease patients' and informal caregivers' lives. Education and guidance of appropriate palliative care interventions to improve symptom control are needed. A case conference intervention with individualised care plans may help in addressing the substantial symptom control and psychosocial needs of these patients and informal caregivers.

Keywords

Pulmonary fibrosis, lung diseases, interstitial, palliative care, qualitative research

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Background

There are at least 5000 new cases of progressive idiopathic fibrotic interstitial lung disease (PIF-ILD) including idiopathic pulmonary fibrosis (IPF) each year in the United Kingdom, with a similar number of deaths.¹ Median survival from diagnosis in the United Kingdom is approximately 3 years.^{2,3} Only a minority of patients are suitable for lung transplantation, and there are no other viable treatment options once the disease is advanced and irreversible.⁴

Previous qualitative studies in the Netherlands⁵ and in the United States⁶ have focussed on identifying factors which may affect Health-Related Quality of Life. In addition, a recent qualitative study focussed on perspectives on the diagnostic process and disease education.⁷ None of these studies aimed to assess in depth the specialist palliative care needs of these patients, and none of these studies interviewed informal caregivers and health professionals. There are large gaps in our knowledge of both the disease experience and specialist palliative care needs of those living with PIF-ILD. Interviewing informal caregivers and health professionals in conjunction with patients may improve this. It is important to get a true picture of the specialist palliative care needs and disease experience before effective palliative care interventions for this disease group can be developed.

This study aims to explore the specialist palliative care needs and disease experience of PIF-ILD patients and informal caregivers while enhancing findings with health professionals' views. Previous data from this study⁸ have shown that PIF-ILD patients and informal caregivers have a poor understanding of prognosis and how the disease will manifest in the end stages. Patients and informal caregivers express a wish to receive more information about the future from clinicians. In addition, patients and informal caregivers rarely have specialist palliative care input and are unlikely to have considered important end-of-life issues, such as preferred place of care and preferred place of death. Data presented here on the symptom control, psychosocial needs and disease experience of patients and informal caregivers will be used with previous data about the end-of-life planning and information needs⁸ to inform and develop a complex intervention at the end of life for patients with ILD and their informal caregivers.

Material and methods

Study design and setting

Semi-structured interviews were conducted among PIF-ILD patients and informal caregivers of dependants or relatives with PIF-ILD attending the Royal Brompton Hospital (RBH) and King's College Hospital (KCH) National Health Service (NHS) Foundation Trusts between December 2010 and March 2011. RBH is a specialist ILD centre in central London. The unit has one of the largest diffuse lung disease patient populations in the world with over 500 new referrals a year

from across London and the surrounding counties. KCH represents a tertiary hospital with a specialist ILD clinic in the south-east of London. KCH serves a geographical area characterised by multiple deprivation in addition to a large population of Black and minority ethnic communities.

Interviews were also conducted among health professionals from RBH, St Christopher's Hospice and those working in primary care. St Christopher's Hospice is part of a palliative care service which delivers palliative care across a number of settings in South London.⁹

Recruitment

We identified patients who fulfilled the following inclusion criteria: a diagnosis of non-specific interstitial pneumonia, IPF and idiopathic interstitial pneumonia as classified by American Thoracic Society/European Respiratory Society (ATS/ERS) criteria¹⁰ with advanced progressive disease (with a percentage predicted transfer factor of the lung for carbon monoxide (TLCO) < 40%), capacity to provide informed consent and ability to understand and speak English fluently.

Those under 18 years of age, with cognitive impairment or those unable to provide informed consent were excluded. Informal caregivers and health professionals involved in the care of these patients were also identified.

S.B. attended ILD clinics to recruit participants. For health professionals, a wide range of multidisciplinary members were sought from both the primary and secondary care settings.

This study was approved by the local ethics committee (South West London Rec 4 REF 09/H0806/74) and written informed consent obtained.

Data collection

A purposive sampling frame was developed to recruit a diverse patient population with respect to age, respiratory or cardiovascular co-morbidities, community palliative care and informal caregiver support. Qualitative sampling strategies are not designed to achieve statistical generalisation or test hypotheses. Instead, qualitative research takes an inductive approach and involves the in-depth study of the range and complexity of meanings and phenomena relevant to the research question, with the aim of providing explanations and conceptual generalisation.¹¹ Although the number of participants in this study is relatively small, it was consistent with the methodological literature concerning in-depth qualitative work where a point of diminishing returns can occur in increasing the sample size which then no longer contributes to new evidence.¹² In view of this, and because this was a small-scale exploratory study, data collection ended.

All interviews were conducted by S.B. who was a palliative care doctor and who had received training in qualitative

research. She had not had any previous contact with the patients or informal caregivers but had developed professional relationships with some of the health professionals (ILD and Palliative Care Consultant). Participants were made aware of the aims of the research, but personal goals and reasons for doing the research were not discussed. This work was conducted as part of a larger PhD project for S.B. The interviews were informal in style and loosely followed a topic guide that was initially guided by review of the literature and a critical review of deceased patients' notes in both units.¹³ This topic guide was piloted prior to use. A list of questions appears in Text Box 1. Similar interview schedules were used for informal caregivers and health professionals. Field notes were made during and after the interviews.

Box 1 - Patient semi-structured interview schedule

- How does your disease affect you? Prompts: physically (symptoms and what helps relieve), psychologically, socially (activities of daily living (ADLs), personal/relationship issues)
- Could you tell me what things are most important for you about your disease?
- What do you feel are the most important things that affect your quality of life?

Analysis

All interviews were audio-recorded, transferred verbatim onto a secure transcription database and then imported into NVIVO 9 software to facilitate analysis using the constant comparative method.¹⁴ Each transcript was subject to line-by-line axial coding by S.B. Codes were scrutinised for internal consistency through an iterative process. Codes and sub-codes were tabulated during the charting process to allow abstraction and synthesis of themes while drawing on a priori issues – those drawn from the original research objectives and the interview schedule. The completed coding frame and sample comparison were reviewed by S.B., J.K. and I.J.H. to confirm the analysis and interpretation. To maximise analytical rigour, a selection of the interviews was also reviewed by a second researcher (J.K.) and consensus achieved.¹⁵ Excerpts from the interview transcripts are presented to illustrate themes. All participants' names have been changed throughout this article to preserve their anonymity.

Results

Sample characteristics

In total, 12 patients were approached during the course of the study. Four declined to be interviewed, two patients did

not feel that they had the energy and two did not have the time. Five informal caregivers were approached and only one declined (he did not want to/feel that he could leave his wife). All health professionals approached agreed to take part in the interview. Eight patient participants (four from RBH and four from KCH), four informal caregivers (from RBH) and six health professionals agreed to be interviewed. In order to maintain anonymity of health professional participants, we provide the following summary description of the six participants: ILD team members (physiotherapist, nurse specialist, consultant), palliative care team members (nurse specialist, consultant), and general practitioner (GP). Ages ranged between 31 and 59 years, and four were men. Five were White British and one White Other. All interviews except one were conducted alone and ranged between 35 min and 1 h in duration. The informal caregivers and patients interviewed had no relationship to each other. The main characteristics of the patient and informal caregiver participants are presented in Table 1.

Findings

Four main themes emerge from the qualitative analysis: (1) the extent of physical and psychosocial needs, (2) health-care professionals' experience of symptom control, (3) impact of disease on social activities and (4) reliance on others and the change in relationships.

The extent of physical and psychosocial needs. This theme relates to the presence and magnitude of the physical and psychosocial needs of these patients. The three main physical symptoms reported by patient participants during the interviews were shortness of breath, cough and difficulty sleeping. In addition, the majority of patient participants also reported psychological problems.

While only one patient reported one symptom, half of patients interviewed reported four or more uncontrolled symptoms that frequently existed in combination. Eight patients reported shortness of breath, five reported depression, five reported cough, three reported difficulty sleeping, two reported anxiety and one reported fatigue.

The physical impact of living with PIF-ILD was commented on by all participants. The concern they shared was that breathlessness was the overwhelming symptom. Many participants stated how their breathlessness had taken on a life of its own and was consuming them. This is illustrated by Ruth:

I'm breathless, always breathless. (Ruth, in her 50s, Black Caribbean IPF patient)

However, some patient participants expressed that even though it was the worst aspect about their illness, they paradoxically felt quite healthy. An example of this includes Jim, an older man in his 70s with advanced IPF, who believed he

Table 1. Description of patient and informal caregiver characteristics (names changed to ensure confidentiality).

Name of participant	Gender	Age	Ethnicity	Diagnosis	TLCO	Co-morbidities	Palliative care involvement	Informal caregiver
Patients								
RBH1 – Terry	Male	81	White British	IPF	38	No	No	No
RBH2 – John	Male	63	Asian	IPF	35	No	No	No
RBH3 – Jim	Male	77	White British	IPF	33	Yes – COPD	No	Yes
RBH4 – Peter	Male	65	White British	IPF	39	No	No	Yes
KCH1 – Mary	Female	75	White British	IPF	36	Yes – osteoporosis	No	Yes
KCH2 – Ruth	Female	56	Black Caribbean	IPF	35	No	No	Yes
KCH3 – George	Male	74	Cypriot	IPF	31	No	No	No
KCH4 – Lea	Female	57	South American	NSIP	30	Yes – rheumatological disease	No	Yes
Informal caregivers								
Gender	Age	Ethnicity	Relationship to patient					
RBHC1 – Penny	Female	63	White British	Wife of James (advanced IPF)				
RBHC2 – Jane	Female	41	White British	Daughter of Anne (advanced IPF)				
RBHC3 – Joan	Female	55	White British	Wife of Paul (advanced IPF)				
RBHC4 – Anthony	Male	63	White British	Husband to Betty (advanced IPF)				

TLCO: percentage predicted transfer factor of the lung for carbon monoxide; RBH: Royal Brompton Hospital; COPD: chronic obstructive pulmonary disease; KCH: King's College Hospital; IPF: idiopathic pulmonary fibrosis; NSIP: non-specific interstitial pneumonitis.

was otherwise well despite his continuous struggle to breathe freely every day. Courageously, he quietly accepted the breathlessness and tried to continue with his everyday life.

Both patients and informal caregiver participants recognised that breathlessness was not an isolated symptom. Instead, it appeared to be far more complex often residing alongside overwhelming anxiety and panic that invariably amplified distress. This is illustrated by Penny, who reported that when she was providing care for her husband James, she noticed that even the mere suggestion of stress or anxiety exacerbated instances of incapacitating breathlessness. Panic was often reported as being an unwelcome companion of breathlessness:

she'll panic because although she tries not to but em she would panic because it's not nice not being able to breathe you know ... (Anthony, husband to Betty)

Importantly, some health professionals also recognised the seriousness of the symptom and its far reaching impact:

the symptom of breathlessness is the most significant symptom that I've come across (...) ... it could mean that they are anxious as well about the breathlessness and about whether this is what it is going to feel like when they die. (ILD physiotherapist)

Desperation resulting from symptom-related distress was a common theme associated with the illness and its progression. Many patient participants highlighted that cough was a common and highly irritating problem. Patients reported that the paroxysms of cough and the considerable effort in trying to bring up phlegm were totally consuming. This left them drained and utterly depleted:

when it's really really bad, I'd make a trade with the devil (...) because I'm so (...) flat and exhausted and [I] think well I'd rather not go on. (Peter, in his 60s with advanced IPF)

Patient such as Lea, who was in her 50s with end-stage non-specific interstitial pneumonitis (NSIP), found it difficult to sleep at night due to her symptoms. This then impacted on her day-to-day life. She felt exhausted and unable to engage in life in any meaningful way. Lea commented that it 'would be a miracle' to have a restful night's sleep and clearly felt desperate that this was something that was highly unlikely to ever happen.

In addition to the physical impact, the disease had considerable impact on patients' psychological well-being. Informal caregivers, for example, Joan, felt that their loved ones often struggled unsuccessfully to come to terms with the disease. This led to corrosive intimations about their future. Joan felt desperate to limit the psychological impact that the disease was having:

He wouldn't have it that there was anything wrong with him. But that's just a thing, but between us we're alright, it just a strain, a constant strain of trying to keep him (...) not happy, but trying to keep him thinking positively and just trying to get through each day and some days it's not too bad and other days it's a real struggle ... he's becoming more and more depressed ... (Joan, in her 50s and wife of Paul)

Health-care professionals' experience of symptom control. Participants from all three groups interviewed reported the challenges in adequately controlling symptoms. This left patient participants, informal caregivers and health professionals all struggling to find solutions. Non-ILD health professionals admitted that they did not possess sufficient

understanding or experience of the disease. This consequently left them feeling poorly equipped to manage or provide guidance to support their patients. Both the GP and palliative care clinical nurse specialist (CNS) were concerned that immediate-release morphine would bring about respiratory depression and more distress and were reluctant to prescribe.

Health professionals who had previously experienced patients with poorly controlled symptoms stated that this had influenced their perception of the disease, the frustration of not being able to adequately manage symptoms and the depressing legacy of their failure:

Um I mean I have never seen quite so much phlegm (laughs nervously) and he was literally choking on it, he was deeply blue and and there was a sense of sort of hopelessness that nobody could actually do anything about it and I thought there probably were few few worse ways to die than that when I saw it in that instant, sort of haunts me a bit today. (Palliative Care Consultant)

However, despite the often bleak fate that patients had to endure, some health professionals still recognised their contribution in improving symptoms. For example,

definitely breathlessness management, I think we are really good at it ... if again you take breathlessness ... and having all those sort of offshoots, of anxiety, function and oxygen we definitely definitely have a benefit, where even if that's to the family as well, the practicalities of managing with a patient with breathlessness we definitely have a role um and one's that been positive. (ILD physiotherapist)

There was clear recognition from all participating health professionals that wherever possible, it was important to attempt to improve the symptoms of these patients, and some recognised that this could be achieved through relatively simple measures:

I still think we can make a major difference to their quality of life through various interventions aimed at symptoms (1) um [...] so certainly the feedback that one gets from patients is that they certainly feel they've gone from being hopeless that that what they were suffering was what they had to suffer and and just through the implementation of some very simple symptom based remedies one can make a big difference to how they feel. (ILD Consultant)

Impact of the disease on social activities. This theme refers to the day-to-day impact of the disease and its associated symptoms in preventing patients getting out and engaging in their interests or hobbies. All participants commented on how their illness had progressively prevented patients from going about their everyday lives. In the early stages, this appeared to be because they were very self-conscious of the symptomatic manifestations of their illness:

Yeah, um, because I'm always coughing when I'm out [...] yeah. You get funny looks thinking okay (slight cough) you know people probably thinking I've got something [...] something you're going to pass on to them cuz I'd probably would think the same. (clears throat) (Ruth, in her 50s, Black Caribbean IPF patient)

However, in the later stages, the limitation on social activities progressed to being more about physical limitations in engaging with previously taken-for-granted activities. Joan described how it had become impossible for her husband Paul to travel on the bus or train because he could not walk very far and would have coughing fits. All three groups commented on the social isolation. Mary, who did not have anyone to take her out on a regular basis, reported how this had led to her becoming separated and lonely:

I can't go anywhere [...] ... I don't don't [really] have a life I'm sitting indoors everyday ... I used to be meet friends and have coffee and it [would] give you a bit of life back ... (Mary, in her 70s with advanced IPF)

Declining physical function and its consequent impact on social activities and hobbies were closely associated with loss. Many like Peter, who was in his 60s and had been recently diagnosed with advanced IPF, had been looking forward to retiring and being able to enjoy these hobbies. He eloquently described how he felt cheated:

I was gardening after 36 years of er er of working in management, and then starting to chop down trees and digging um holes in the ground in the open country side, the sun beating down and all the plants, and everything, I was loving every moment of it and now I can hardly get into my own garden, I bend down to do pull a weed out, I have to take 10 minutes to get up off my knees again ... (Peter, in his 60s with IPF)

Reliance on others and change in relationships. This last theme refers to the increasing loss of independence patients were required to adapt to, the resultant changes in their relationships with close others and how health professionals attempted to understand their new circumstances. Jim, a patient in his 70s with advanced IPF, was now heavily dependent on his wife to perform tasks of a very intimate nature, such as washing and tending to parts of his body that were now inaccessible to him. Both this greater reliance on loved ones and the nature of the tasks they were called upon to perform led to dramatic and interesting changes in dynamics between patients and informal caregivers that now needed to be accommodated. Many patients felt isolated, lonely and lacking purpose, and their identities were consumed by their illness. Peter, a man in his 60s with advanced IPF, who had always been fiercely independent and the one to look after his family illustrates this in the following:

Peter: ... you never think that you are going to get in a position where you um you can't look after um everybody else (upset).

S.B.: (9) that's obviously quite upsetting for you?

Peter: mmm. (6) (blows nose, upset). (19) It only when I talk to you like this um makes you realise that um how dependent really I I am on the family. Although um I try not to be um when you talk sit down and think about it I I am very dependent on them.

Informal caregivers, such as Anthony, who was the husband and sole carer to Betty, recognised that it is paramount for the ill patient to still feel that he or she had a legitimate role in everyday family life and that his or her status be it as wife, husband or as any other had not been taken away. By deliberately remaining close at hand, Anthony enabled his wife Betty, a woman with advanced IPF, to continue to cook most of their meals. This touching act was an open acknowledgement of that was intended to reaffirm her continued importance in their relationship. However, other informal caregivers, such as Joan who was in her 50s and wife of Paul who had advanced IPF, found it more challenging to find the right balance:

... where I find it difficult is I want to do everything for him. You tend to want to say no you stay there you sit there, don't move, I'll do it, and then that makes him cross as well and he keeps saying 'I'm not dead yet' ... (Joan, wife of Paul)

Many informal caregivers described how the experience of illness had led to a corrosive strain on their relationships with others especially their spouse. Informal caregivers like Penny, wife of James, struggled to adapt to the increasing reliance of her husband on her time and emotional well-being. She felt suffocated and frustrated by his neediness. Other informal caregivers reported that they often took the brunt of the bad moods and sometimes struggled to cope:

he gets um I told you, very touchy, very [...] angry and obviously I'm the only one around, um so from that point of view we do argue more um, (3) so I suppose yes it did, it's made it very difficult from the point of view of that, um where he um [...] he can't cope with it, and I'm there, so he'll tend to vent whatever he's feeling at me, um verbally or [...] you know [...] I just won't talk um so it is a strain, it it puts a strain on the whole relationship really (SIGH) ... sometimes he gets quite emotional about it all, and other times he gets quite nasty. (Joan, wife of Paul)

Marital relationships were affected in other ways too. This included moments of sexual intimacy. Ruth eloquently described how the illness had affected the deepest and most sensitive depths of their relationship, which neither of them acknowledged, but it was always there unspoken, not dealt with and highly distressing. She said,

Ruth: ... we're not intimate at the moment (higher pitch voice) because I find it (...) we don't even talk about it, we just sort of blank it out because I just don't have the (1) the will or the energy to do (slight laugh) anything ... Having intercourse, you know and you know, making love with each other and that sort of thing, yeah ... I just don't have the energy but (...) we just don't talk about it.

S.B.: And how do you, how does that make you feel?

Ruth: Frustrated I suppose, annoyed (clears throat).

Importantly, the effects of the disease on informal caregivers and relationships were not always felt to be recognised by health professionals:

I think we underestimate the eh impact that it has on the carers, relatives, [their] relationship (...) relations who live with the family and I think they equally worry and I think that is a cause of concern for patients as well as the family and I think that's underestimated by us. (ILD CNS)

Discussion

This qualitative study explored the specialist and complex palliative care needs of PIF-ILD from the perspective of patients, their informal caregivers and health professionals. Many patient participants reported that the main symptoms associated with PIF-ILD were shortness of breath, cough and insomnia. This finding has correspondence with results from the retrospective component of our study¹³ and a previous qualitative study in the United States.⁶ However, our study progresses the evidence base by identifying that the burden these symptoms imposed on patients is even more profound than previously noted.^{6,7} While these concerns were voiced by all patients and their informal caregivers, health professionals differed in their perspective: they sometimes departed from patient- and family-centred concerns and had a more limited appreciation of these symptoms and their psychosocial effects. Research suggests that health-care professionals' attitudes often dominate patients' responses to their experience of some symptoms.^{16,17} Health-care professionals have therefore been criticised for patronising patients by ignoring their 'illness narratives' or the meanings that govern how they understand and accommodate their illness.¹⁸ Illness narratives should therefore be viewed by health and social care professionals as an important source of information in the overall process of arriving at a more complete picture of a clinical problem. The consequences of neglecting this on patients' and their informal caregivers' lives warrant attention.

The most common symptom experienced was shortness of breath. There were similarities to other disease groups' experiences of shortness of breath. Shortness of breath as a

reminder of one's mortality has been seen in chronic obstructive pulmonary disease (COPD) patients, disability with social isolation and depression has been seen in heart failure patients and anxiety/panic associated with bad episodes is similar to that previously seen in motor neuron disease (MND) patients.¹⁹ However, our study also showed a more pronounced strain in spousal relationships. The palliative 'total care' model aims to offer high-quality care not just to the patients but also to their spouses, partners or other close relatives or friends. Informal caregivers provide invaluable support to patients and often enable them to stay in their preferred place of care.

The findings from this qualitative study identify that informal caregivers populate a unique position: they not only provide invaluable care but they *also* potentially need support in order to continue in their role. Our study shows that PIF-ILD informal caregivers experience the disease with substantial unmet psychosocial needs. This is similar to the disease experiences of spouses of cancer patients where it has been recognised that even though spouses assume a pivotal role, their needs are frequently overlooked.²⁰ Previous work done has also shown that the vast majority of PIF-ILD patients are dying in hospital.¹³ While support for informal caregivers has been addressed in part in the cancer population towards the end-of-life,^{21,22} there is limited research into effective interventions for informal caregivers in the ILD population.²³ Interventions targeted at improving psychosocial support of informal caregivers may improve the quality of life of both patients and informal caregivers while enabling these patients to remain at home in the later stages of their disease.

Finally, there seemed to be resignation among some health professionals that patients would inevitably suffer poor symptom control. This appeared to be partly due to some health professionals' lack of knowledge and misconceptions of effective symptom control interventions. This deficit in the knowledge on how to assess and then manage distressing symptoms is critical. Early symptom control interventions have been shown to improve the quality of life of both patients²⁴ and informal caregivers.²⁵ This may be most appropriate through the introduction of evidence-based guidelines and may empower health professionals treating PIF-ILD patients to deliver effective specialist palliative care where they have not previously felt confident to do so.

Other data collected from these participants have shown that patients and informal caregivers experience unmet end-of-life planning needs, poor coordination of care and dissatisfaction with communication.⁸ Case conferencing may provide a mechanism to improve these unmet needs.²⁶ In adapting this model for PIF-ILD patients, it is possible that the use of evidence-based symptom control guidelines may also help develop an individualised care plan effectively addressing the

physical and psychosocial needs of these patients and informal caregivers. This may help improve the gaps noted in this study and previous studies.⁸

There are limitations to this study. First, the number of subjects interviewed is small. However, through integration of data from the three groups of participants, the elaboration and enhancement of findings have contributed to rigour. Second, all subjects had a TLCO less than 40% indicating severe, if not terminal, disease. There can be marked heterogeneity in progression within the disease population. However, there are clear needs in all these patients and informal caregivers. Future work may explore data more widely across the disease trajectory and potentially longitudinally. Finally, all patients and informal caregivers were recruited from specialist ILD centres in the United Kingdom. Patients and informal caregivers attending non-specialist respiratory clinics may have different specialist palliative care needs to the ones recruited in this study. The findings are, however, in agreement with previous works done internationally.^{5,6}

Conclusion

This study is the first of its kind to examine in depth the impact of symptom control and psychosocial needs revealing the profound effect on every aspect of PIF-ILD patients' and informal caregivers' lives. Health professionals feel less confident in dealing with the symptom control needs of these patients, and the psychosocial needs of both patients and informal caregivers are not currently being met. Education and guidance of appropriate palliative care interventions to improve symptom control are needed. A case conference intervention with individualised care plans may help in addressing the substantial symptom control and psychosocial needs of these patients and informal caregivers.

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Declaration of conflicting interests

There are no competing interests for any of the authors.

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4.4.3.2 Further results of qualitative findings related to *identifying/developing theory* phase.

Four main themes emerge from the qualitative analysis: 1) The extent of physical and psychosocial needs 2) Healthcare professionals' experience of symptom control 3) Impact of disease on social activities and 4) Reliance on others and the change in relationships.

4.4.3.2.1 Theme 1 The extent of physical and psychosocial needs.

This theme relates to the presence and magnitude of the physical and psychosocial needs of these patients.

The physical impact of living with PIF-ILD was commented on by all participants. The concern they shared was that breathlessness was the overwhelming symptom. Many participants stated how their breathlessness had taken on a life of its own and was consuming them. This is illustrated by Ruth:

'I'm breathless, always breathless' (Ruth, in her 50s, black Caribbean IPF patient)

However, some patient participants expressed that even though it was the worst aspect about their illness, they paradoxically felt quite healthy. An example of this includes Jim, an older man in his 70s with advanced IPF, who believed he was otherwise well despite his continuous struggle to breathe freely every day. Courageously, he quietly accepted the breathlessness and tried to continue with his everyday life.

Both patients and informal caregivers recognised that breathlessness was not an isolated symptom. That is that it was multi-factorial and could be precipitated by anxiety. Penny, in caring for her husband James, had noticed that when there was even a slight question in his mind or any anxiety or frustration, such as not being able to get his computer to work or not being able to find his pen, resulted in episodes of incapacitating breathlessness. Panic was often reported as being an unwelcome companion of breathlessness:

'she'll panic because although she tries not to but em she would panic because it's not nice not being able to breathe you know...' (Anthony, husband to Betty)

Patients and informal caregivers recognised that the disease appeared to have control over them both physically and socially and no matter what they did things did not improve and this was difficult to come to terms with. Importantly, some HPs also recognised the seriousness of the symptom and its far reaching impact:

'the symptom of breathlessness is the most significant symptom that I've come across (...)...it could mean that they are anxious as well about the breathlessness and about whether this is what it is going to feel like when they die.' (ILD Physiotherapist)

Desperation resulting from symptom related distress was a common theme associated with the illness and its progression. Cough was also a significant problem with paroxysms or coughing fits leading to headaches and difficulty sleeping at night noted by many patients including George, Jim and Peter. The considerable effort in trying to bring up phlegm was totally consuming. This left them drained and utterly depleted:

'when it's really really bad, I'd make a trade with the devil (..) because I'm so (..) flat and exhausted and [I] think well I'd rather not go on.' (Peter, in his 60s with advanced IPF)

Patients such as Lea, who was in her 50s with end stage NSIP, found it difficult to sleep at night due to her symptoms. This then impacted on her day to day life. She felt exhausted and unable to engage in life in any meaningful way. Lea commented that it 'would be a miracle' to have a restful night's sleep and clearly felt desperate that this was something that was highly unlikely to ever happen.

As well as the physical impact, the disease had considerable impact on patients' psychological well-being. Informal caregivers, for example Joan, felt that their loved ones often struggled unsuccessfully to come to terms with the disease. This led to corrosive intimations about their future. Joan felt desperate to limit the psychological impact that the disease was having:

'He wouldn't have it that there was anything wrong with him. But that's just a thing, but between us we're we're alright, it just a strain, a constant strain of trying to keep him (...) not happy, but trying to keep him thinking positively and just trying to get through each day and some days it's not too bad and other days it's a real struggle... he's becoming more and more depressed...' (Joan, in her 50s and wife of Paul)

4.4.3.2.2 Theme 2 Healthcare professionals' experience of symptom control

Participants from all three groups interviewed reported the challenges in adequately controlling patients' symptoms. However, patient and informal caregiver participants reported few symptom control interventions with little or no use of pharmacological and non-pharmacological interventions. This left patient, informal caregivers and HP participants all struggling to find solutions. Non ILD HP participants admitted they did not possess sufficient understanding or experience of the disease. This consequently left them feeling poorly equipped to manage or provide guidance to support their patients. Both the GP and Palliative Care CNS were concerned that immediate release morphine would bring about respiratory depression with more distress and were reluctant to prescribe.

HP participants who had previously experienced patients with poorly controlled symptoms stated this had influenced their perception of the disease, the frustration of not being able to adequately manage symptoms and the depressing legacy of their failure:

'Um I mean I have never seen quite so much phlegm (laughs nervously) and he was literally choking on it, he was deeply blue and there was a sense of sort of hopelessness that nobody could actually do anything about it and I thought there probably were few few worse ways to die than that when I saw it in that instant, sort of haunts me a bit today.' (Palliative Care Consultant)

However, despite the often bleak fate that patients had to endure some HP still recognised their contribution in improving symptoms. For example.....

'...definitely breathlessness management, I think we are really good at it... if again you take breathlessness...and having all those sort of offshoots, of anxiety, function and oxygen we definitely definitely have a benefit, where even if that's to the family as well, the practicalities of managing with a patient with breathlessness we definitely have a role um and one's that been positive.' (ILD physiotherapist)

There was clear recognition from all participating HPs that wherever possible it was important to attempt to improve the symptoms of these patients and some recognised that this could be achieved through relatively simple measures.

'I still think we can make a major difference to their quality of life through various interventions aimed at symptoms (1) um (...) so certainly the feedback that one gets from patients is that they certainly feel they've gone from being hopeless that that what they were suffering was what they had to suffer and and just through the implementation of some very simple symptom based remedies one can make a big difference to how they feel.' (ILD Consultant)

However, other HP did not have much understanding or experience of the disease which left them unconfident and needing guidance in addressing treatment in these patients.

4.4.3.2.3 Theme 3 Impact of the disease on social activities

This theme refers to the day to day impact of the disease and its associated symptoms in preventing patients getting out and engaging in their interests or hobbies. All participants commented on how their illness had progressively prevented patients from going about their everyday lives. In the early stages, this appeared to be because they were very self-conscious of the symptomatic manifestations of their illness. Ruth described how she had stopped going out because of her embarrassment about her cough and fear that people would feel that she had a disease that was 'catching':

'Yeah, um, because I'm always coughing when I'm out (...) yeah. You get funny looks thinking okay (slight cough) you know people probably thinking

I've got something (...) something you're going to pass on to them cuz I'd probably would think the same. (clears throat)' (Ruth, in her 50s, black Caribbean IPF patient)

However, in the later stages the limitation on social activities progressed to being more about physical limitations in engaging with previously taken for granted activities. Joan described how it had become impossible for her husband Paul to travel on the bus or train because he couldn't walk very far and would have coughing fits. All three groups commented on the social isolation this led to and again the dependence on loved ones to function on a day to day basis. Anthony, husband of Betty, expressed how Betty was cut off in her own home and needed either Anthony or their sons to take her out or she would not be able to go anywhere. For others such as Mary, who did not have anyone to take them out on a regular basis, this had led to her becoming separated and lonely with a loss of previous relationships which had in turn impacted on her mood:

' I can't go anywhere (...) because I I just get breathless,..... I don't don't [really] have a life I'm sitting indoors everyday...I used to be meet friends and have coffee and it [would] give you a bit of life back...' (Mary, in her 70s with IPF)

Declining physical function and its consequent impact on social activities and hobbies was closely associated with loss. Many like Peter who was in his 60s and had been recently diagnosed with advanced IPF, had been looking forward to retiring and being able to enjoy these hobbies. He eloquently described how he felt cheated:

'I was gardening after 36 years of er er of working in management, and then starting to chop down trees and digging um holes in the ground in the open country side, the sun beating down and all the plants, and everything, I was loving every moment of it and now I can hardly get into my own garden, I bend down to do pull a weed out, I have to take 10 minutes to get up off my knees again...' (Peter, in his 60s with IPF)

4.4.3.2.4 Theme 4 Reliance on others and change in relationships

This last theme refers to the increasing losses of independence patients were required to adapt to, the resultant changes in their relationships with close others, and how HPs attempted to understand their new circumstances.

In addition to the symptom issues, there was an overwhelming effect on mobility which also led to a loss of independence and a reliance on others for basic activities of daily living such as washing and dressing. Mary, who was in her 70s with advanced IPF but also had co-existing osteoporosis, described how she was no longer able to do any housework nor to wash and dress herself and was totally reliant on her daughter. Patients like Jim, in his 70s with advanced IPF, was now heavily dependent on his wife to perform tasks of a very intimate nature; washing and tending to parts of his body that were now inaccessible to him. Both this greater reliance on loved ones, and the nature of the tasks they were called upon to perform, led to dramatic and interesting changes in dynamics between patients and informal caregivers that now needed to be accommodated. Many patients felt isolated, lonely and lacking purpose and their identities were consumed by their illness. Peter, a man in his 60s with advanced IPF, who had always been fiercely independent and the one to look after his family illustrates this:

‘.....you never think that you are going to get in a position where you um you can’t look after um everybody else (upset).’ (Peter, in his 60s with advanced IPF)

SB – (9) that’s obviously quite upsetting for you?

‘mmm. (6) (blows nose, upset). (19) It only when I talk to you like this um makes you realise that um how dependent really I I am on the family. Although um I try not to be um when you talk sit down and think about it I I am very dependent on them.’ (Peter, in his 60s with advanced IPF)

Informal caregivers such as Anthony, who was husband and sole carer to Betty, recognised that it was paramount for the ill patient to still feel they had a legitimate role in everyday family life and their status be it as wife, husband etc had not been taken away. By deliberately remaining close-at-hand Anthony enabled his wife Betty, a woman with advanced IPF, to continue to cook most of their meals. This touching act was an open acknowledgement of that was intended to

reaffirm her continued importance in their relationship. However, other informal caregivers like Joan who was in her 50s and wife of Paul who had advanced IPF, found it more challenging to find the right balance:

'....where I find it difficult is I want to do everything for him. You tend to want to say no you stay there you sit there, don't move, I'll do it, and then that makes him cross as well and he keeps saying "I'm not dead yet"...'
(Joan in her 50s, wife of Paul)

Many informal caregivers described how the experience of illness had led to a corrosive strain on their relationships with others, especially their spouse. Informal caregivers like Penny, wife of James, struggled to adapt to the increasingly reliance of her husband on her time and emotional well-being. She felt that he would not let her do anything on her own, even for half an hour, as he was scared for himself. Other informal caregivers such as Joan often took the brunt of the bad moods and sometimes struggled to cope. Joan recognised the impact of the disease and the strain on their marital relationship when Paul would often react in different ways emotionally which was unpredictable and left her drained:

'he gets um I told you, very touchy, very (...) angry and obviously I'm the only one around, um so from that point of view we do argue more um, (3) so I suppose yes it did, it's made it very difficult from the point of view of that, um where he um (...) he can't cope with it, and I'm there, so he'll tend to vent whatever he's feeling at me, um verbally or (...) you know (...) I just won't talk um so it is a strain, it it puts a strain on the whole relationship really (SIGH)... sometimes he gets quite emotional about it all, and other times he gets quite nasty.' (Joan in her 50s, wife of Paul)

Marital relationships were affected in other ways too. This included moments of sexual intimacy. Ruth eloquently described how the illness had affected the deepest and most sensitive depths of their relationship, which neither of them acknowledged, but it was always there unspoken, not dealt with and highly distressing. She said:

'we're not intimate at the moment (higher pitch voice) because I find it (...) we don't even talk about it, we just sort of blank it out because I just don't

have the (1) the will or the energy to do (slight laugh) anything.....Having intercourse, you know and you know, making love with each other and that sort of thing, yeah.....I just don't have the energy but (...) we just don't talk about it.' (Ruth, in her 50s, black Caribbean IPF patient)

SB: And how do you, how does that make you feel?

'Frustrated I suppose, annoyed (clears throat).' (Ruth, in her 50s, black Caribbean IPF patient)

Informal caregivers clearly worried about their loved ones and many HPs including the ILD CNS felt this worry and the impact of the disease on the informal caregiver were underestimated by HPs. Importantly, the effects of the disease on informal caregivers and relationships was not always felt to be recognised by HPs:

'I think we underestimate the eh impact that it has on the carers, relatives, [their] relationship (...) relations who live with the family and I think they equally worry and I think that is a cause of concern for patients as well as the family and I think that's underestimated by us.' (ILD CNS)

4.4.3.3 Implications for the requirements of a palliative intervention from the qualitative work in *identifying/developing theory* phase

The qualitative work from the *identifying/developing theory* stage has indicated that in adapting the H2H model, guidance and education in delivery in symptom control to this group of patients is needed. Secondly, an adapted H2H model would need to focus on addressing both the physical and psychological symptoms. Finally, an adapted H2H model would need to maximise support to informal caregivers to aim to alleviate some of the psychosocial burden.

4.4.4 Presentation of the qualitative findings related to the *modelling theory and processes* phase

In this section I will initially present the results from the qualitative interviews relating to the *modelling theory/process* phase of the MRC guidance. This is the same data set as the results presented in section 4.4.4. I will first present the published paper followed by the more detailed results. Finally, I will discuss what the findings from the qualitative results presented indicate would be needed from the adapted H2H intervention.

4.4.4.1 Bajwah S, Koffman J, Higginson IJ, Ross JR, Wells AU, Birring SS, Riley J. “I wish I knew more....” - the end-of-life planning and information needs for end-stage fibrotic interstitial lung disease: views of patients, informal caregivers and health professionals. *BMJ Supportive & Palliative Care* 2013;3:84-90

'I wish I knew more ...' the end-of-life planning and information needs for end-stage fibrotic interstitial lung disease: views of patients, carers and health professionals

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ABSTRACT

The importance at the end of life of developing effective communication and meeting information needs is recognised as being central to enhance patient and family centred experience. This qualitative study aimed to explore understanding of the disease, preferences regarding end-of-life planning, and views on communication and coordination of care in patients with Progressive Idiopathic Fibrotic Interstitial Lung Disease (PIF-ILD). Twelve semistructured in-depth qualitative interviews were conducted among PIF-ILD patients and carers attending two London hospitals. Six Interviews were also conducted among health professionals from one London Hospital, a palliative care service and primary care. There was good understanding of the terminal nature of the disease among both patients and carers, but a poor understanding of prognosis, and how the disease would manifest at the end stages. Both patients and carers expressed a wish to receive more information from clinicians. Health professionals recognised the difficulty of balancing information needs with maintaining hope. No participants were aware of any palliative care input, and no participants had considered important end-of-life issues, such as preferred place of care and preferred place of death. Our work shows that palliative interventions need to be developed for this group of patients which should aim to improve communication and coordination of care, while facilitating discussions surrounding information needs and important end-of-life preferences.

INTRODUCTION

There are at least 5000 new cases of progressive idiopathic fibrotic interstitial lung disease (PIF-ILD), including idiopathic pulmonary fibrosis (IPF) each year in the UK, with a similar number of deaths.¹ Median survival from diagnosis in the UK is approximately 3 years.^{2,3} Only a minority of patients are suitable for lung transplantation, and there are no other viable treatment options once the disease is advanced and irreversible.⁴

PIF-ILD patients are reviewed in general and specialist respiratory clinics. The vast majority of their care is provided in the acute hospital setting. There is currently a deficiency in referral to palliative care services despite a high symptom burden and poor prognosis.⁵ In addition, nearly all these patients will die in hospital with repeated hospital admissions in the last year of life.⁵ There is a clear need to deliver effective end-of-life care.⁵

Research conducted in other non-malignant disease groups has identified that there is very little, or no discussion, between patients, carers and health professionals directly addressing patients' and carers' concerns.^{6,7} This, in turn, has been shown to affect psychological morbidity.⁸ Quantitative analysis of the perceptions of illness in IPF patients and their family members in one study is limited, as numbers were small (n=32), but has shown that most patients understand their disease to be a 'serious condition', and that family members understand the patient might not survive (n=16).⁹ Another quantitative study has shown that patients and carers in the USA feel there was a lack of information at the time of diagnosis.¹⁰ Qualitative methods have been shown to provide a richness of data, with emergent theories, and allow the researcher to delve deeply into issues.¹¹ Previous qualitative studies in patients with IPF have shown significantly impaired health-related quality of life.^{12,14} However, none of these studies have involved carers and health professionals. Interviewing carers and health professionals would allow a deeper understanding of the issues involved and triangulation of findings. In addition, there have been no qualitative studies to explore PIF-ILD patients' end-of-life preferences/planning and information needs. This information is central to enhancing end-of-life interventions.

This qualitative study aimed to explore (1) patients' and carers' understanding of their disease (specifically in areas surrounding prognosis), (2) patients' and carers' preferences regarding end-of-life planning and (3) patients', carers' and health professionals' views on communication and coordination of care.

MATERIAL AND METHODS

Study design and setting

Semistructured interviews were conducted among PIF-ILD patients and carers attending the Royal Brompton (RBH) and Kings College Hospital (KCH) NHS Foundation Trusts between December 2010 and March 2011. RBH is a specialist ILD centre in central London. The unit has one of the largest diffuse lung disease patient populations in the world, with over 500 new referrals a year from across London and the surrounding counties. KCH represents a tertiary hospital with a specialist ILD clinic in the southeast of London. KCH serves a geographical area characterised

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by material and social deprivation, in addition to a large population of black and minority ethnic communities.

Interviews were also conducted among health professionals from RBH, St Christopher's Hospice and those working in primary care. St Christopher's Hospice is part of a palliative care service which delivers palliative care across a number of settings in South London.¹⁵

Recruitment

We identified patients who fulfilled the following inclusion criteria: a diagnosis of non-specific interstitial pneumonia, IPF and idiopathic interstitial pneumonia, as classified by the American Thoracic Society/European Respiratory Society criteria¹⁶ with a percentage-predicted transfer factor <40%, and an ability to understand and speak English fluently. Carers and health professionals involved in the care of these patients were also identified.

A purposive sampling frame was developed to recruit a diverse patient population with respect to age, respiratory or cardiovascular comorbidities, community palliative care and carer support. SB attended ILD clinics to recruit participants. Those under 18 years of age with cognitive impairment, or those unable to provide informed consent, were excluded. For health professionals, a wide range of multidisciplinary members was sought from both the primary and secondary care setting.

The study was approved by the local ethics committee, and written informed consent obtained.

Data collection

The interviews were informal in style, and loosely followed a topic guide that was initially guided by review of the literature. This topic guide was piloted prior to use. Interviews began with a general discussion about what patients understood by their disease and its prognosis, and then progressed to explore end-of-life preferences and communication-related issues. Prompts were used to elicit further information. A list of questions appears in box 1. A similar adapted interview guide was used for carers and health professionals.

Analysis

All interviews were audio-recorded, transferred verbatim onto a secure transcription database, and then imported into NVIVO 9 software to facilitate analysis using the constant comparative method.¹⁷ Each transcript was subject to line-by-line axial coding by SB. Codes were scrutinised for internal consistency through an iterative process. Codes and subcodes were tabulated during the charting process to allow abstraction and synthesis of

themes. The complete coding frame and sample comparison were reviewed by SB, JK and IJH to confirm the analysis and interpretation. To maximise analytical rigour, a selection of the interviews was reviewed by a second researcher (JK), and consensus achieved.¹⁸ Excerpts from the interview transcripts are presented below, to illustrate themes. All participants' names have been changed to preserve anonymity.

RESULTS

Sample characteristics

Twelve patients were approached during the course of the study. Four declined to be interviewed; two patients did not feel that they had the energy, and two did not have the time. Five carers were approached and only one declined (he did not wish to leave his wife). All health professionals approached agreed to take part in the interview. Eight patient participants (four from RBH and four from KCH), four carers (from RBH) and six health professionals agreed to be interviewed. The health professionals comprised an ILD physiotherapist, ILD clinical nurse specialist (CNS), ILD consultant, community palliative care CNS, palliative care consultant and a general practitioner. All interviews, except one, were conducted alone. The carers and patients interviewed had no relationship with each other. The main characteristics of the patients and carers are presented in table 1.

Findings

Five main themes emerged from the qualitative analysis: (1) making sense of the inexplicable; (2) end-of-life information needs; (3) sources of information; (4) end-of-life planning, decision making and care and (5) coordination of care.

Making sense of the inexplicable

Patients and carers held varying views of what their illness meant to them. For example, Penny described how her husband who had advanced IPF had become fixated on his health since becoming ill. She recognised that the disease was at the forefront of his mind and that he needed to keep talking about it, but she felt that it had taken over his life.

He talks about his health quite a lot ... we can be talking about something completely different and it's suddenly back to (...) to the health ... (Penny, wife of James).

Patients, such as Peter, in his 60s and with advanced IPF were shocked at the profound changes the disease had brought to their physical state. Consequently, they had considerable difficulty coming to terms with the loss of who they had been and what they had now become:

Looking at myself in a full length mirror and seeing those legs that used to score 20 goals a season, look as those they are a pair of (...) match sticks, so the weight, not weight loss, muscle loss in my legs came comes as a shock to me ... (Peter).

Ruth, a younger Black Caribbean woman in her 50s, could not fully understand the rapid deterioration in her health. She felt challenged by the lack of control:

You know (2) it's just (...) really frustrating to tell you the truth (1) these things are happening to my body (...) that I can't do anything about it (higher pitch voice). (Ruth).

Patients and carers all appeared to understand that the disease was affecting the lungs and restricting ability to breathe, but had limited understanding of the exact mechanism

Box 1 Patient semistructured interview schedule

- ▶ What is your understanding of your disease and how do you see your illness progressing in the future?
- ▶ Have you made any decisions about your treatment and care when you are less well?
- ▶ What do you think about current communication between health professionals?
- ▶ What do you think about information provided to you about the disease?
- ▶ Have you made any plans for when you are less well/end of life?

Table 1 Description of participant characteristics (names changed to ensure confidentiality)

Name of participant	Gender	Age	Ethnicity	Diagnosis	TLCO	Comorbidities	Palliative care involvement	Informal caregiver
Patients								
RBH1 Terry	Male	81	White British	IPF	38	No	No	No
RBH2 John	Male	63	Asian	IPF	35	No	No	No
RBH3 Jim	Male	77	White British	IPF	33	Yes, COPD	No	Yes
RBH4 Peter	Male	65	White British	IPF	39	No	No	Yes
KCH1 Mary	Female	75	White British	IPF	36	Yes, osteoporosis	No	Yes
KCH2 Ruth	Female	56	Black Caribbean	IPF	35	No	No	Yes
KCH3 George	Male	74	Cypriote	IPF	31	No	No	No
KCH4 Lea	Female	57	South American	NSIP	30	Yes, rheumatological disease	No	Yes
Carers						Relationship with patient		
RBHC1 Penny	Female	63	White			Wife of James (advanced IPF)		
RBHC2 Jane	Female	41	White			Daughter of Anne (advanced IPF)		
RBHC3 Joan	Female	55	White			Wife of Paul (advanced IPF)		
RBHC4 Anthony	Male	63	White			Husband to Betty (advanced IPF)		

COPD, chronic obstructive pulmonary disease; KCH, Kings College Hospital; IPF, idiopathic pulmonary fibrosis; RBH, Royal Brompton; TLCO, percentage-predicted transfer factor.

involved, its poor prognosis, or how the disease may manifest in the end/terminal stages. Most participants understood the gravity of the diagnosis, but this realisation had been gradual. Joan, in her 50s, and wife of Paul, who had rapidly advancing IPF, reported her realisation had been precipitated by the gradual deterioration in Paul's health, rather than any information provided. As Paul found it increasingly harder to cope, this had forced them both to accept that he was never going to improve, and that death '*was not going to be pleasant*'.

End-of-life information needs

All participants shared a common sentiment about the lack of information to help plan for the future. For example, two patients, Jim and Peter, both wished they knew more about their disease and its likely outcome. Central to this was a wish to understand exactly how they would deteriorate at the end of life. This is best illustrated by Jim who was aware he knew very little about his fate, but at the same time felt ambivalent about wanting to ask health professionals for information; he explained he was deeply apprehensive about their reply, and had, at times, wanted to remain in the dark:

I haven't sort um I haven't really discussed (1) um (2) how it will develop with anybody, but you know that may be me own fault um if I don't talk about it, to somebody, and you don't know then I've got nothing to worry about (laughs). (Jim).

Importantly however, patients wanted to have the option of gathering further information, and being able to discuss issues, if they wished, which they did not feel was currently the case.

All carers wanted to know more about their dependants' situation, but also wanted to maintain hope. Health professionals recognised the importance of delivering information:

Empowering the patient with information about what their disease is (...) eh ... what's likely to happen and the treatment so you're involving them very early on so they have a good understanding of the whole ... (...) package of what's wrong with them. I think that is the single most import thing that we can do (...) eh to help them to understand. (ILD consultant).

However, health professionals also recognised the complexities of delivering information in their attempt to preserve a balance between hope and realism:

I think sometimes the delivery is wrong (...) which could be a problem. Um what you don't want to do is completely say 'you're going to die' what you want to do is give them some hope ... (ILD CNS).

Sources of information

Despite health professionals recognising the importance of providing clear and complete information to patients to best prepare them for their end of life, patients and carers had resorted to obtaining information from other sources. For example, Jane, who had lived with her mother, Anne (advanced IPF) for much of her adult life, had been the one to break the news of the poor prognosis. She had found this distressing:

Myself and my husband got on the internet and found out 'well actually life spans 5 years,' she had no idea, no one's even told her that (...) so we go 'how do we tell her this' (...) so actually the actual breaking the news was myself ... (Jane).

Health professionals recognised this was occurring and the pitfalls of this:

I think that the healthcare professionals involved tend to ... (...) tell patients verbally a lot of information, but that's not the same as having written information that they can take away, digest and share with their family ... they'll go and look it up on the internet and read lots of horror stories perhaps (...) and I think what we should be better at is providing our own ... written information (ILD consultant).

The actual timing of information was a concern for both patients and health professionals. Patients felt that health professionals should be able to best judge when discussions about end-of-life planning, and care should take place, as they had developed experience in undertaking these difficult conversations. However, health professionals had reservations:

People often um have (1) um (4) you know attend clinics where there's decisions taken about their management um but (2) maybe not um enough thought and enough time is given to giving them (1) information really about things.' (Palliative Care consultant).

End-of-life planning, decision making and care

No patients, and no patients cared for by the carers, reported they had formulated end-of-life plans, or considered end-of-life

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preferences, such as preferred place of care or preferred place of death. A number of carers were aware of broad preferences, but in-depth conversations had not occurred. All patients, and all carers, realised the importance of such conversations, but did not know how to initiate conversations with their loved ones.

Worryingly, some participants, like Peter, held unrealistic perceptions of how they were likely to die, which had led them to not consider important end-of-life preferences:

SB: Have you made any decisions about how you want to be looked after?

(2) In the time leading up to the big day? No no I haven't in that respect except that um no I haven't because I don't expect to be looked after, I just expect sooner or later I'm going pop off the edge of the cliff. So I won't need looking after. (Peter).

No patients, or carers, reported palliative care involvement stating that they were not aware of any such services. All health professionals felt that there was still an association of palliative care with malignant disease, and a failure to appreciate that fibrotic lung disease towards the end stage behaves much like malignant disease and causes unpleasant symptoms. However, all health professionals felt that all patients should be referred earlier for palliative input, and have more symptom control interventions. Interestingly, health professionals recognised when faced with a patient, they were not always aware of the need to deliver symptom control.

The patients get used to the breathlessness, their doctors and nurses get used to the breathlessness, and (...) the penny doesn't drop that maybe they need to have um (I) to use drugs for the symptomatic relief of breathlessness. (GP).

Coordination of care

Patients and carers reported being very satisfied with the specialist respiratory care received. However, communication between health professionals and coordination of care was flagged as a problem by all participants. Penny, wife of James stated:

I think they try to liaise between each other but it so often falls apart ... there is really a short coming amongst um getting information from one aspect of the medical profession to the other.

And also by Jane, daughter of Anne, whom it had clearly affected:

The breakdown of communication over in [local hospital] has been (...) dreadful for someone who's got (...) supposedly um ... you know a terminal illness, it's been dreadful.

This sentiment was supported by health professionals who were frustrated at poor communication, and recognised that vast improvements were needed to ensure adequate coordination of end-of-life care.

We need to really (...) review the way we think about people who've got (...) um rapidly progressive non malignant disease or people who've got who are literally dying from non malignant disease, the kind of communication we expect around cancer (...) really should happen around (...) these other diseases, so take IPF (...) um (...) ... I think that the quality of communication has got to be a lot better, these people don't get treated properly ... (GP).

DISCUSSION

This qualitative study aimed to explore understanding of PIF-ILD, preferences regarding end-of-life planning and views on communication and coordination of care. This study adds to previous quantitative knowledge in these areas, and highlights

important issues surrounding end-of-life preferences, inadequate information provision, and poor communication.

We identified a good general understanding from both patients and carers that PIF-ILD is a serious illness which is terminal. This finding supports what has been noted in a previous quantitative study.⁹ Interestingly, in our study, this realisation appeared to be a gradual process, and often precipitated by deterioration in health rather than any formal information provided. As a result, they were not adequately prepared, nor had they considered important end-of-life issues.

There is no previous literature on end-of-life planning and decision making in this disease group. In our study, no patients had made end-of-life plans. In addition, carers had not had conversations concerning end-of-life decisions, such as preferred place of care and preferred place of death with their loved ones. This supports similar findings in other non-malignant diseases, such as heart failure.⁸ Challenges were apparent. First, some carers did not know how to broach the subject. Second, patients had unrealistic perceptions of how their disease would progress, and what the terminal stages would manifest as. These led to unrealistic perceptions that they would not need care or help at the end of life. However, the willingness of participants to discuss their preferences was clear.

Clinicians caring for patients with PIF-ILD face a challenging task regarding information needs for both patients and carers. They are a group of conditions that the general public is, on the whole, unfamiliar with, and so, natural introductions to questions regarding prognosis and end-of-life care are usually not initiated by patients themselves. By contrast, with malignant disease, this places the onus for developing such conversations almost completely with the healthcare professional, in the main, a respiratory physician. In the context of busy clinic appointments, during which information regarding diagnosis, treatment options and medical care also have to be communicated, it is not surprising that the uncomfortable topic of end-of-life care is neglected. However, this study shows the importance that patients and their carers place on these issues.

Previous studies have identified that patients are often prescribed subtherapeutic doses of information; a recent quantitative survey of IPF patients and carers conducted in the USA reported that two-thirds of respondents felt there was a clear lack of information.¹⁰ In the cancer setting, clinicians tend to underestimate the amount of information that patients require.^{19 20} In fact, a large multicentre UK cancer study (2331 patients) showed that 87% of participants wanted to know all information, both good and bad news.²¹ In our study, all patients and carers felt that information provided about the future was lacking and could be improved. All health professionals recognised the importance of providing information about prognosis and end of life, with accurate prognostication and timely conversations to ensure that patients and carers had the opportunity to make end-of-life plans. Despite this, many carers reported receiving information from other sources, for instance, the internet; the delivery of difficult news that the disease was terminal was not from the doctor. Patients and carers felt it was the health professionals' responsibility to provide them with information, and to be able to judge what information should be provided, and when. However, health professionals did not feel that this was done well. In addition, many patients in the cancer setting assume that the doctor would have told them everything relevant.²² This was similar to our study, where patients were trusting in the skills of doctors. Literature repeatedly states that patients have high information needs and wish to be kept well informed about

their illness regardless of diagnosis.^{23 24} However, while the physical care skills of respiratory clinicians may well be excellent, this is not necessarily the case as far as effective communication of end-of-life issues are concerned.²⁵ It may be the case that there is a purposeful non-disclosure of information which may result from poor training, or a lack of awareness of the impact that a failure to disclose has on patients and carers.²⁵ Our study showed that patients and carers wanted to know, but might be too afraid to ask. Clinicians need to anticipate this, and continuously assess patients' and carers' information needs throughout the disease trajectory, and although discussions about prognosis in time-pressured clinics are difficult, healthcare professionals can learn effective communication skills to assist them in delivering this information sensitively.^{26 28} There is an increasing case for properly resourced ILD services to be developed, similar to those provided for patients with lung cancer, in which a specialist nurse and early palliative care involvement is easily accessible. This study supports such a model.

It has been noted that there is inadequate communication between health professionals.²⁹ Our study also found that there was poor communication between the acute and primary care setting leading to frustration for patients, carers and health professionals alike. There was also a feeling that malignant diseases had much better communication surrounding end-of-life issues than was currently being seen in PIF-ILD patients. It is not clear whether this is due to non-recognition of the terminal phase, or inadequate provision for communication.

There are a few limitations to this study. The number of subjects interviewed is small. However, analysis showed no further new themes emerging, suggesting that there would have been no benefit to conducting further interviews. In addition, through integration of data from the three groups of participants, the triangulation of findings has contributed to rigour. All subjects had a percentage-predicted transfer factor less than 40%, indicating severe, if not terminal, disease. There can be marked heterogeneity in progression within the disease population. However, there are clear needs in all these patients and carers. The cross-sectional design of the study did not allow for exploration of the progression of end-of-life planning and information needs with time. Despite aiming to recruit patients who had palliative care input, and those who did not, this was not possible, as very few patients attending the clinics had been referred to palliative care. All patients and carers were recruited from specialist ILD centres. Patients and carers attending non-specialist respiratory clinics may have different end-of-life planning and information needs to the ones recruited in this study.

This is the first study to explore preferences regarding end-of-life planning and communication between patients, carers and health professionals on end-of-life issues in this group of patients. Our work shows that any palliative interventions developed should aim to improve communication and coordination of care, while facilitating discussions surrounding information needs and end-of-life preferences. Further research is needed to develop specific interventions and care pathways, and to evaluate outcomes for patients and carers that include end-of-life planning and communications needs.

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4.4.4.2 Further results of qualitative findings related to modelling *theory and processes* phase

Six main themes emerged from the qualitative analysis: (i) Making sense of the inexplicable (ii) End of life care information needs (iii) Sources and timing of information (iv) End of life planning, decision making and care (v) Co-ordination and satisfaction with current care (vi) Views of the H2H CC model of care

4.4.4.2.1 Theme 1 Making sense of the inexplicable

Patient and informal caregiver participants held varying views of what their illness meant to them. For example Penny described how her husband who had advanced IPF had become fixated on his health since becoming ill. She recognised that the disease was at the forefront of his mind and that he needed to keep talking about it but she felt that it had taken over his life:

'he talks about his health quite a lot... we can be talking about something completely different and it's suddenly back to (...) to the health...' (Penny, wife of James.)

Patients such as Peter, in his 60s with advanced IPF, were shocked at the profound changes the disease had brought to their physical state. Consequently, they had considerable difficulty coming to terms with the loss of who they had been, and what they had now become:

'looking at myself in a full length mirror and seeing those legs that used to score 20 goals a season, look as those they are a pair of (...) match sticks, so the weight, not weight loss, muscle loss in my legs came comes as a shock to me...' (Peter, in his 60s with IPF)

Ruth, a younger Black Caribbean woman in her 50s, could not fully comprehend the rapid deterioration in her health. She felt challenged by the lack of control:

'you know (2) it's just (...) really frustrating to tell you the truth (1) these things are happening to my body (...) that I can't do anything about it (higher pitch voice).' (Ruth, in her 50's, black Caribbean IPF patient)

Patients and informal caregiver participants all appeared to understand that the disease was affecting the lungs and restricting ability to breathe but had limited understanding of the exact mechanism involved or how the disease may manifest in the end/terminal stages. Most participants understood the gravity of the diagnosis but this realisation had been gradual. Joan, in her 50s and wife of Paul, who had rapidly advancing IPF, reported her realisation had been precipitated by the gradual deterioration in Paul's health rather than any information provided. As Paul found it increasingly hard to cope, this had forced them both to accept that he was never going to improve and that death 'was not going to be pleasant'.

Interestingly, patients or informal caregivers rarely knew about prognosis. Informal caregivers such as Jane, who was in her 40s and daughter of Anne who had advanced IPF, had researched the disease and were aware that there was no cure but understandably wanted to try and maintain hope. Jane was particularly close to her mother having only moved out of the family home two years previously:

'I think because I've researched it so much we've become very real about the disease... we=you know we're not living in fairyland, we're not looking, we'd love there to be something, there's always that grasping at straws and that glimmer of hope that something will (.) materialise that may... so she can feel that she's actually doing something rather than waiting for something to happen.....' (Jane, in her 40s and daughter of Anne who had advanced IPF)

Both patients and informal caregiver participants had little understanding of how the disease may manifest in the end/terminal stages and how they may eventually die. Patients such as Jim, who was in his 70s and suffered from IPF for 2 years and COPD for a number of years, thought that he would get more and more short of breath and then die of 'oxygen starvation'. Most patients and informal caregiver participants admitted to not having any idea what would happen.

4.4.4.2.2 Theme 2 End of Life Care information needs

All participants shared a common sentiment about the lack of information to help plan for the future. For example two patients, Jim and Peter, both wished they knew more about their disease and its likely outcome. Central to this was a wish to understand exactly how they would deteriorate at the end of life. This is best illustrated by Jim who was aware he knew very little about his fate, but at the same time felt ambivalent about wanting to ask HPs for information; he explained he was deeply apprehensive about their reply and had at times wanted to remain in the dark:

'I haven't sort um I haven't really discussed (1) um (2) how it will develop with anybody, but you know that may be me me own fault um if I don't talk about it, to somebody, and you don't know then I've got nothing to worry about (laughs).' (Jim, in his 70s, with advanced IPF)

Importantly however, patient participants wanted to have the option of knowing further information about their condition and being able to discuss issues if they wished which they did not feel was currently the case.

All informal caregiver participants wanted to know more about their dependants' situation but also wanted to maintain hope. HP participants recognised the importance of delivering information:

'empowering the patient with information about what their disease is (...) eh... what's likely to happen and the treatment so you're involving them very early on so they have a good understanding of the whole... (...) package of what's wrong with them. I think that is the single most important thing that we can do (...) eh to help them to understand.' (ILD Consultant)

However, HP participants recognised the complexities of delivering information to patients and that this required an appropriate balance of hope and realism. They also recognised that this was not always done well:

'I think sometimes the delivery is wrong (..) which could be a problem. Um what you don't want to do is completely say 'you're going to die' what you want to do is give them some hope (.) I mean for example in IPF, which is a good example of this, you want to say that 'you may be able to try and stabilise (.) um the disease with eh... with treatments' um but you have to also... sort of balance that with you know 'things may not get any better'So there's a balance to be had and some physicians are better at it than others.....' (ILD CNS)

4.4.4.2.3 Theme 3 Sources and timing of information

Despite HPs recognising the importance of providing information to patients in preparation for the end of life, patients and informal caregivers were often getting information from other sources such as the internet. Jane, who had lived with her mother Anne for much of her adult life, had been the one to break the news of the poor prognosis to her mother which she had clearly found difficult and distressing:

'myself and my husband got on the internet and found out 'well actually life spans 5 years,' she had no idea, no one's even told her that (...) so we go 'how do we tell her this' (...) so actually the actual breaking the news was myself and my husband not the consultant to say, 'well actually there isn't a cure for this.' (Jane, in her 40s and daughter of Anne who had advanced IPF)

HP participants recognised this was occurring and the pitfalls of this:

'I think that the healthcare professionals involved tend to... (...) tell patients verbally a lot of information, but that's not the same as having written information that they can take away, digest and share with their family...they'll go and look it up on the internet and read lots of horror stories perhaps (...) and I think what we should be better at is providing our own... written information' (ILD Consultant)

The timing of information was commented on by both patient and HP participants. Patients such as Peter felt that HP should be able to judge what information was appropriate and when it should be delivered, not the patient. Peter had a great deal of faith in his doctors and felt a great deal of trust that they would be able to judge when that time had come as they had done it many times before. However, HPs such as the Palliative Care Consultant did not feel that this was done with no allocated responsibility being a contributing factor. This resulted in patients and informal caregivers being left ill informed:

'I think the other problem is that in some ways it is nobody's clear responsibility to do this, and therefore people often um have (1) um (4) you know attend clinics where there's decisions taken about their management um but (2) maybe not um enough thought and enough time is given to giving them (1) information really about things.' (Palliative Care Consultant-Community)

4.4.4.2.4 Theme 4 End of life care planning, decision making and care.

No patient participants and no patients cared for by the informal caregiver participants reported they had formulated end-of-life care plans or considered end-of-life care preferences such as preferred place of care or preferred place of death. A number of informal caregiver participants were aware of broad preferences but in-depth conversations had not occurred. All patient participants and all informal caregiver participants realised the importance of such conversations but did not know how to initiate conversations with their loved ones.

Worryingly, some patient participants like Peter held unrealistic perceptions of how they were likely to die which had led them to not consider important end of life preferences:

SB – have you made any decisions about how you want to be looked after?

'(2) in the time leading up to the big day? No no I haven't in that respect except that um no I haven't because I don't expect to be looked after, I just expect sooner or later I'm going pop off the edge of the cliff. So I won't need looking after. ' (Peter, in his 60s with IPF)

No patient or informal caregiver participants reported palliative care involvement stating that they were not aware of any such services. All HPs felt that there was still an association of palliative care with malignant disease and a failure to appreciate that fibrotic lung disease towards the end stage behaves much like malignant disease and causes unpleasant symptoms. However, all HP participants felt that all patients should be referred earlier for palliative input and have more symptom control interventions. Interestingly, HP participants recognised that respiratory physicians were not always aware of or had confidence in delivering effective symptom control:

'the patients get used to the breathlessness, their doctors and nurses get used to the breathlessness, and (..) the penny doesn't drop that maybe they need to have um (1) to use drugs for the symptomatic relief of breathlessness.' (GP)

There was a clear feeling that the focus of care at the end of life should be in the community rather than the secondary or tertiary care setting but that this wasn't always possible due to a lack of confidence/provision of resources in the community. This was expressed by the patients, informal caregivers and HPs alike. The ILD Consultant explained that the patients were kept in the secondary/tertiary care setting out of necessity:

'I think in most cases it is relatively straight forward to recognise when we've reached the limit of (..) what we can achieve medically, er and I think the major incentive for keeping patients under hospital care is to try and provide some supervision of the end of life (..) to ensure that they are at least getting some management of that, whereas in an ideal situation I think that would transfer (..) fully to the community with us providing a sort of backbone of hospital based setting just providing back up for unexpected complications or disease developments..... patients often I find like to come and see us (..) over and above their secondary care provider or their GP and my perceptions the reason for that are are really that when they come here they see a whole team of nurses, physios, OTs, social workers who are (..) who understand pulmonary fibrosis....' (ILD Consultant)

Clearly HP participants such as the ILD Consultant and ILD CNS felt that PIF-ILD patients needed support in the community at the end of life above and beyond that of seeing the GP. There was a universal view across HP participants that there was poor end of life care for these patients. None of the patient participants or any of the loved ones cared for by the informal caregiver participants had palliative care involvement and all the HP participants felt that this was rare. All HP participants felt that there was still an association of palliative care with malignant disease and a failure to appreciate that pulmonary fibrosis towards the end stage behaves much like a malignant disease and causes unpleasant symptoms towards death. This had contributed to a lack of referrals. HP participants felt that all patients should be referred earlier for palliative input and have more symptom control interventions. All HP participants felt that there appeared to be an inconsistency across the group on whether patients were referred and this affected their overall management and end of life care. Interestingly, HP participants recognised that respiratory physicians were not always aware of or had confidence in delivering effective symptom control interventions:

'My perception is that again with malignant disease I think people are well trained now to recognise (..) when it's reached a point when medical treatment is futile, I think in interstitial lung disease that's much less well recognised even though we know that the sort of physiological parameters that indicate (..) the patient has less than 6 months to live, I think there is a failure to sort of use that to trigger um palliative (..) end of life treatment for these patients. Er and I think that's particularly so when patients are of an age that they can be considered for transplant and that's almost a double edged sword. I mean the list of the transplant people almost don't want to provide to palliative treatments yet we know that over half the patients on the transplant waiting list will die of their disease and won't be transplanted, so (..) I don't think we the respiratory community are very well switched on to the management of these patients.' (ILD Consultant)

All HP participants recognised the importance of accurate prognostication and timely conversations to ensure that patients and informal caregivers had the opportunity to make end of life plans. However, these did not appear to be occurring.

4.4.4.2.5 Theme 5 Co-ordination and satisfaction with current care

The vast majority of patient and informal caregiver participants were happy with the care from the specialist centres. However, involvement of the GP was limited and 2 patients (Jim and Lea) said that they were not happy with care from the GP and did not feel confident in going to them for management of their PIF-ILD. This was supported by Joan, wife of Paul, who felt that the GP appeared disinterested as Paul was under the care of a specialist hospital and Jane, daughter of Anne, who felt that the GP was ill-informed about the disease as she had needed to provide him with written information about the disease.

There was poor multi-disciplinary team involvement with a minority of the patients seeing respiratory nurses in the community (2/8) and no patients had been referred to occupational therapists or physiotherapists in the community. There were also concerns about continuity of care with inconsistencies of provision of support which informal caregivers such as Jane worryingly felt reflected a lack of concern:

'there's no continuity and when you see so many different people who (1) don't even know who you are (..) then you really don't feel that anyone cares (slight laugh) at all to be honest..' (Jane, in her 40s and daughter of Anne who had advanced IPF)

In addition, both patients and informal caregivers felt that PIF-ILD was not a priority compared to other diseases such as cancer and COPD and this frustration was expressed by Peter:

'my opinion, in answer to your question that pulmonary fibrosis is (..) um (..) no let's say let's say nowhere near a priority and I think it's nowhere near a priority because so much or so little is known about it and at the same time, the bit that is known is the bit that they can't do anything about it and so that's why it's not a priority.' (Peter, in his 60s with IPF)

Informal caregivers such as Penny, wife of James, expressed that they would like to know more information about the services that were available as she felt completely in the dark. Penny also mentioned that it would be helpful to have an appropriate point of contact in the community as she did not feel that this was available or certainly had not been communicated to her and she and her husband would find that comforting. Joan, wife of Paul, reiterated that she would like

clarification of what to do or who to contact in an emergency and it had clearly been something that had been playing on her mind:

'sometimes you think (LAUGHS) who would I phone, who would I speak to, would I, if I was panicking, obviously I'd have to phone my own doctor he's nearer, but if I wanted information, I don't know that I would get it from him, he'd probably say to phone you, it's, it's, that's a grey area there, there could be a bit more done there, bit more (..) information from here, to say um you can contact this person or that person if you need to, and this is here, and possibly from our own doctors to say well this is (..) in place, but then perhaps if I went down and made an issue then they would tell me all that information, I don't know, you know, it's just sometimes you (..) can't be bothered (LAUGHS).' (Joan in her 50s, wife of Paul)

HPs such as the physiotherapist and ILD CNS felt that earlier referral to physiotherapy would improve care and symptom control and that overall there was under referral for this disease group. This was supported by patients such as Peter who had found it extremely helpful to attend pulmonary rehabilitation but had been referred 15 months after diagnosis:

'I should have been on the pulmonary the rehab when I got the diagnosis. Because I found things out in the pulmonary in the rehab that I didn't know about and I spent 15 months with the disease, so things were (1) arse about face would be the term....I've been I've gone on 15 months with things happening to me, that I didn't understand for me until part of the education sector of the section of the rehab explained it to me something as simple as breathing exercises, (2) that's had a major impact on me um (2) you know when I've been struggling I now know just how to do breathing control I've gone 15 months not knowing how, crazy.' (Peter, in his 60s with IPF)

Worryingly, some patients and informal caregiver participants felt they didn't know enough about the disease, symptom control and services that should be available to comment on satisfaction of the current services available to them.

Communication between HPs and co-ordination of care was flagged as a problem by all participants. Penny, wife of James stated:

'I think they try to liaise between each other but it so often falls apart..... there is really a short coming amongst um getting information from one aspect of the medical profession to the other. ' (Penny, in her 60s, wife of James with advanced IPF)

And also by Jane, daughter of Anne, whom it had clearly affected:

'the breakdown of communication over in [local hospital] has been (...) dreadful for someone who's got (...) supposedly um... you know a terminal illness, it's been dreadful. '(Jane, in her 40s and daughter of Anne who had advanced IPF)

This sentiment was supported by HP participants who were frustrated at poor communication and recognised that vast improvements were needed to ensure adequate co-ordination of end of life care:

'we need to really (...) review the way we think about people who've got (...) um rapidly progressive non-malignant disease or people who've got who are literally dying from non-malignant disease, the kind of communication we expect around cancer (...) really should happen around (...) these other diseases, so take IPF (...) um (...)....I think that the quality of communication has got to be a lot better, these people don't get treated properly....'GP

4.4.4.2.6 Theme 6 Views of the H2H CC model of care

It was recognised by HP participants such as the Palliative Care Consultant and GP that there needed to be changes to the current model of communication in end of life care for PIF-ILD patients to bring it into line with the standard of communication that was expected in other end of life care diseases such as cancer:

'I think communication tends to take place mostly by letter um which is a sort of after you see somebody in clinic or at home or something like that, which (2) is helpful to some extent, but also I think [it] has its limitations in the sense that um (2) you you tend to deal with single particular problems at particular points in time, um, but there is no kind of communication that I've ever been involved in, that sort of stands back from things a bit and says ok, what are the issues with these people, or even with somebody in particular, and, um tries to get the bigger picture and put some planning into place. So it's always, you are always dealing with crisis management to some extent. You know you are always dealing with um (1) problems as they happen, but there's never a chance to stand back and see the big picture and do things like, say ok have these issues of end of life care [have] been addressed properly for example, um whose going to do it, um you know clarify what everybody roles are, and that kind of thing.' (Palliative Care Consultant)

When described to them, the vast majority of patient, informal caregiver and HP participants felt that the model of the H2H intervention was an excellent one and were overwhelmingly supportive of it. Informal caregiver participants such as Joan, wife of Paul admitted to panicking and not knowing what to do when Paul became short of breath. She could only foresee this getting worse in the future but felt that if she clearly knew a plan of action or who to contact, that this would help both her and Paul. Patients such as Jim explained that at the moment if he was to get breathless and he panicked, he would have no option but to call '999' as both him and his wife would not know 'what else to do'. In addition, health care professional participants such as the ILD CNS felt that clearly allocated roles and responsibilities which were communicated across the board would be helpful in ensuring that all HPs took appropriate responsibility when necessary. The GP interviewed recognised that the CC model of care would facilitate the GP to

take a more prominent role in the end of life care of the patient whilst being supported by other HPs in the community.

Very few concerns were made about the model of care but one included the difficulty of being able to get all the HPs to attend a CC at the same time which was raised by the Palliative Care Consultant who was overall extremely supportive of the idea. There was a hesitation from one patient (Lea) and this was concerning her confidence in her GP. She did not feel that her GP would be able to manage the care in the community (even with support) and expressed that she would not want to transfer the focus of her care from secondary care to primary care.

Other points made by patients and informal caregiver participants included that flexibility in the service would be needed to accommodate people who did not wish to have a great deal of input initially but may do at a later stage and also if people had other co-morbidities, then these HPs would also need to be represented at the CC.

4.4.4.3 Implications for the requirements of a palliative intervention from the qualitative work in *modelling theory and process* phase

The findings from the qualitative interviews used in the *modelling theory and process* have indicated a number of requirements of an adapted H2H model. An adapted H2H model would need to ensure that all the patients' and informal caregivers' information needs are met, it would need to address any unrealistic perceptions and where appropriate facilitate end of life care decisions. Finally, an adapted H2H model would need to facilitate and co-ordinate care, whilst improving communication and allocating clear points of contact for patient and informal caregivers for a change in clinical state/emergencies.

4.5 Discussion

4.5.1 Theoretical perspective

This qualitative work is in a group of people with a progressive disease with no cure. Many of these patients and informal caregivers are initially under the impression that this is a chronic disease. Both patients and informal caregivers have gradual realisation of the seriousness of the disease and this journey is often difficult. These are ordinary people trying to manage a problem. The problem has a physical basis and patients struggle to come to terms with the physical changes and symptoms but this is not always the identity that patients like to present to the world and to their loved ones. Social relationships are central to the formation of an individual's identity and self-hood with others.(146) This perspective underlies this qualitative work which attempts to show how people with PIF-ILD try to understand and cope with the loss of individual identity and threats to social relationships. Bury (147) describes the concept of "biographical disruption" in describing the disease and the concept that the disease represents an assault not only on the person's physical self, but also on the person's sense of identity, calling into doubt the person's self-worth. Bury discusses how the meaning of illness lies in its consequences and significance.(148) The consequences of the disease are certainly very important in the initial stages. That is, the physical impact with the symptoms and change in body image. However, as the disease progresses, the significance of the disease becomes more important. The disease had a profound influence on how patients regarded themselves and they struggled to come to terms with the loss of who they had been and loss of identity. This qualitative work describes a story of an illness concept which Lopowski (149) described as the view that illness is an "irreparable loss". Coping in this instance refers to the kind of behaviour and meaning which people have constructed around their experience of having PIF-ILD. Internal control means having the conviction that one can influence the outcome.(150) Internal control conviction tends to be more concerned with active coping strategies and a greater sense of satisfaction with life, whereas the externalisation of responsibility tends to have less favourable effect.(151) However, there was a distinct lack of internal control expressed by PIF-ILD patients and this appeared to distress the patients greatly. Patients described a lack of control over the disease and the frustrations associated with this. This is referred to not only in the physical aspect but also the social aspect. Thoits (152) discusses how a range of relationships provides people with a set of positive identities. This set of identities in turn is used

as a set of data for a person to use in shaping the self, providing a basis for a sense of control and a feeling of well-being. Coping refers to the cognitive processes whereby the individual learns how to tolerate or put up with the effects of illness.(148) Coping in the sense of maintaining a feeling of personal worth and a “sense of coherence” in the face of disruption has been seen as an important buffer against the stress of chronic illness.(153) Very few patients during these qualitative interviews appeared to be coping with their disease. PIF-ILD appeared to be disruptive to the patients on both a physical and cognitive level. Living with PIF-ILD appeared to weigh heavily on the emotional equilibrium of patients and informal caregivers. With patients finding it difficult to cope with the physical changes, sustaining relationships with family and friends and coping with the loss of social relationships and identity. Normalisation from this viewpoint, a form of coping, may refer to the psychological “bracketing off” of the impact of the illness, so its effects on the person’s identity remain slight.(148) In that sense, very few patients and informal caregivers had normalised the disease. In fact, many patients (both reported by the patients themselves and by the informal caregivers), worried about their disease to the extent that PIF-ILD had taken a dominant role in the identity of the patients. In addition there appeared to be a failure to legitimise the disease in the patients’ life. That is a failure to maintain a sense of personal integrity, and reduce the threat to social status.(148) The use of the term strategy suggests the need for dynamic view of choice and constraint, as people attempt to weigh up alternative forms of action.(148)

4.5.2 Discussion of methods

The Framework method of analysis provided me clear steps to produce highly structured outputs of summarised data which can could then be interrogated.(134) This does not suggest the currency of the findings are of little worth. Indeed, a number of recent studies that have utilised this approach have made important contributions to sociological theory.(154, 155) In addition, Framework analysis has been used effectively in clinical research aimed at developing interventions.(156, 157) At all stages, steps were taken to maximise rigour and validity. For example, where themes/categories were not immediately apparent, I repeatedly followed the stages of data analysis with reflection and reviewing the data from different perspectives to ensure high quality findings. When considering which method of qualitative analysis to use, unquestionably the nature of Framework analysis was intuitively appealing as it provided clear

structure for me as a 'first time' qualitative researcher. However, it also allowed me to use both a deductive approach to the analysis, with themes and codes preselected (based on the literature and discussion with experts on the Project Advisory Group) and an inductive approach which allowed themes to be generated from the data independent of the coding framework. I believe this has not only provided me with data which is rich and a meaningful reflection of patients' and informal caregivers' needs and experiences, but also importantly data that are still relevant to my research aims.

4.5.3 Limitations

There are limitations to this qualitative component of the study. First, the number of participants interviewed was relatively small. However, through integration of data from the three groups of participants, the elaboration and enhancement of findings has contributed to rigour and the credibility of the finding I present. Second, all subjects had a TLCO less than 40% indicating severe, if not terminal, disease. There can be marked heterogeneity in progression within the disease population. However, there are clear needs in all these patients and informal caregivers. Future work may explore data more widely across the disease trajectory and potentially longitudinally. In recruiting informal caregivers, I did not automatically use patient and informal caregiver dyads. In hindsight, this may have been an easier way to recruit informal caregivers. Finally, all patients and informal caregivers were recruited from specialist ILD centres in the UK. Patients and informal caregivers attending non-specialist respiratory clinics may have different specialist palliative care needs to the ones recruited in this study. The findings are however, in agreement with previous conducted internationally.(37, 38)

4.5.4 Summary of findings for *modelling theory and process* phase

In this section, I will model theory and process to be used in the **Feasibility and Piloting** stage. To do this, I will present the findings from the systematic review and qualitative interviews which relate to the *modelling theory/process* stage of the MRC guidance. I will then show how these results have been incorporated to adapt the H2H CC model of care for PIF-ILD. Finally, I will discuss how the systematic review and qualitative work have informed the outcomes that will be used for the **Feasibility and Piloting** stage.

4.5.4.1 Summary of finding from systematic review

In developing and evaluating a palliative intervention developed from the systematic review, I would need to use primary outcome measures related to symptom control and QoL and if possible use a RCT model of evaluation.

4.5.4.2 Summary of findings of specialist palliative care needs from retrospective review and qualitative work

A summary of the specialist palliative care needs identified in both the retrospective review of medical notes and the qualitative work is shown in Table 4-6 Page 180.

Table 4-6 Summary of specialist palliative care needs identified from retrospective review of medical notes and qualitative work during Development phase

Specialist palliative care needs		Development phase
Physical	Shortness of breath	RRM & Qual
	Cough	RRM & Qual
	Pain	RRM
	Fatigue	RRM & Qual
Psychosocial	Anxiety	RRM & Qual
	Depression	RRM & Qual
	Insomnia	RRM & Qual
	Support for informal caregiver	Qual
End of life planning	Including discussions surrounding Preferred Place of Care and Death	RRM & Qual

RRM= Retrospective Review of Medical notes Qual=Qualitative work

An adapted H2H model of care will therefore need to:

1. Address the symptom control needs of the patient and psychosocial needs of patient and informal caregiver
2. Address the information needs of the patients and informal caregivers in a sensitive and individualised manner
3. Address end of life decisions and end of life planning where appropriate

4. Allocate clear points of contact for patient and informal caregivers for a change in clinical state/emergencies
5. Educate and guide HPs on the symptom control of these patients
6. Invite other disease groups to the CC

4.5.5 Integration of the background and qualitative work to adapt the H2H model

The current cancer model of H2H is set up to address aims 2-4. By conducting the H2H CC in PIF-ILD, this is likely to increase the profile of PIF-ILD within the community. In addition, education about the study and the intervention will also do this. Other disease groups are not normally invited to the H2H CC but this can be incorporated into the model. However, education and guidance of appropriate palliative care interventions to improve symptom control are needed. An appropriate way to do this may be to provide HPs involved with evidence based guidelines at the CC for the symptom control of these patients. Guidelines provided from a specialist centre may help allay some of the concerns and confidence issues. In addition, it may ensure some uniformity to the palliative care delivered. Guidelines for the symptom control of patients with PIF-ILD were therefore developed which have incorporated the limited evidence base for PIF-ILD with standard palliative care treatments (APPENDIX B). Graphical depiction of the adapted H2H model is shown in Figure 4- Page 182.

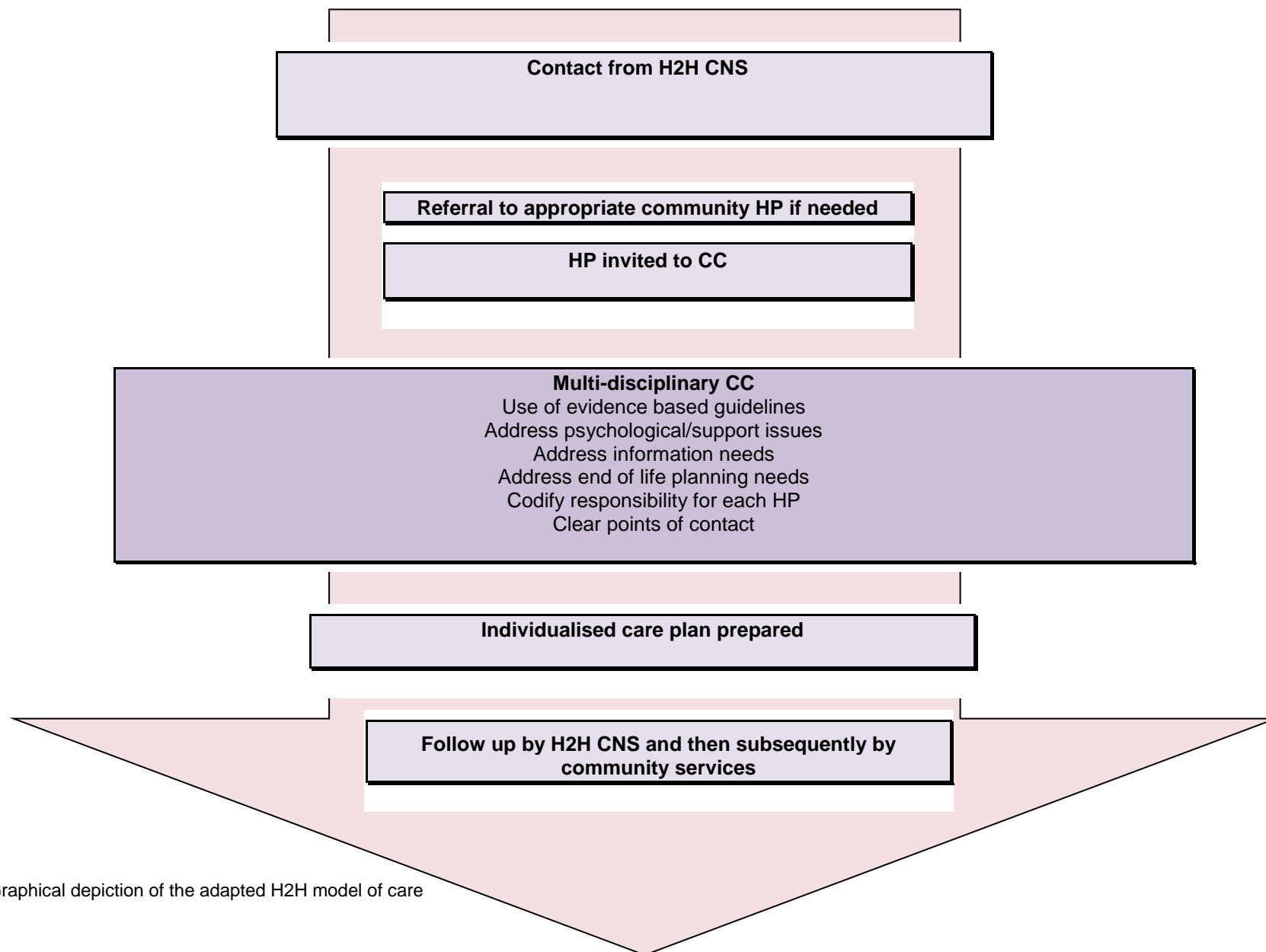


Figure 4-3 Graphical depiction of the adapted H2H model of care

4.6 Conclusion

This chapter includes research that adds to the evidence base forming part of the *identifying/developing* theory stage of the Development stage of the MRC framework. The palliative care needs of those living with PIF-ILD assessed through qualitative work were presented and resultant recommendations for adaption of the H2H model of care.

I have taken findings from the background work, systematic review and qualitative work to develop and adapt the model of H2H to be used in PIF-ILD. I will now present the methods, results and discussion from the RCT in the **Feasibility and Piloting** stage.

Chapter 5 Randomised Controlled trial- Feasibility and Piloting

stage of the MRC guidance

5.1 Introduction

This chapter will form the **Feasibility and Piloting** stage of the MRC guidance. I will initially present aims of the RCT and then the submitted paper followed by more detailed methods, results and discussion.

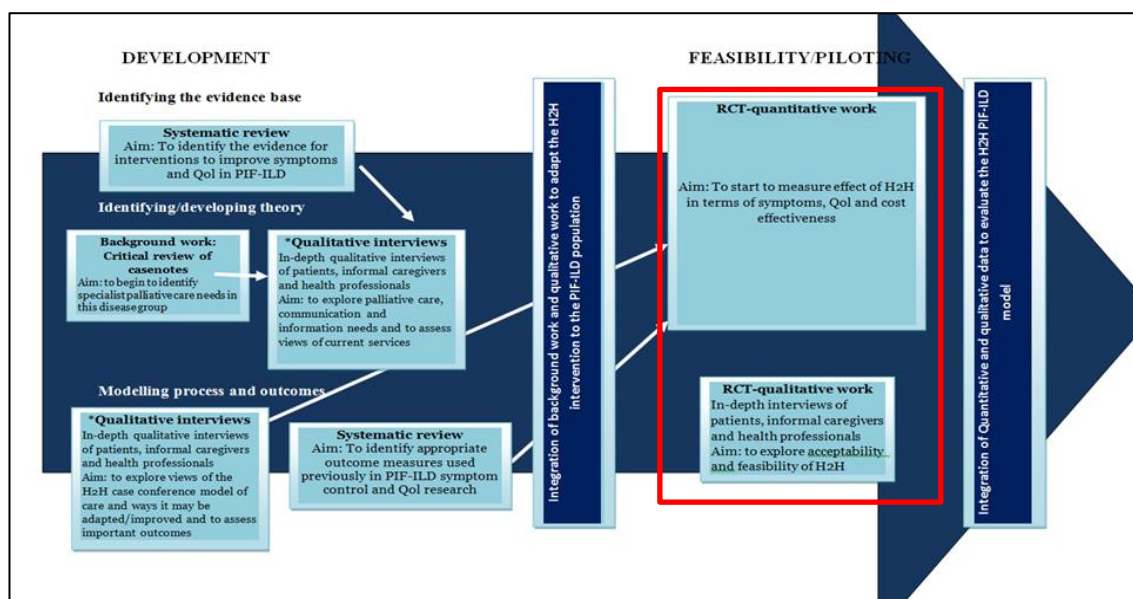


Figure 5-1 Figure showing RCT to be presented in overall plan of study

5.2 Aims of RCT

- To define appropriate outcomes and measures for the adapted H2H intervention.
- To begin to evaluate H2H in a phase II study
- To evaluate the intervention in terms of feasibility and acceptability in a phase II study.
- To use the above work to inform a future larger randomised controlled trial (RCT phase III/**Evaluation** trial).

5.3 Bajwah S, Ross JR, Wells AU, Mohammed K, Oyeboode C, Birring SS, Koffman J, Higginson IJ, Riley J. Palliative Care for Patients with Advanced Fibrotic Lung Disease: a randomised controlled phase II and feasibility trial of a case conference intervention. Thorax doi:10.1136/thoraxjnl-2014-206583

ORIGINAL ARTICLE

Palliative care for patients with advanced fibrotic lung disease: a randomised controlled phase II and feasibility trial of a community case conference intervention

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ABSTRACT

Background Those affected by advanced fibrotic interstitial lung diseases (ILDs) have considerable unmet symptom and psychological needs. Case conferencing has been proposed to address these issues, but requires evaluation.

Aim To obtain preliminary information on the impact of a case conference intervention delivered in the home (Hospital2Home) on palliative care concerns of patients and their carers, and to evaluate feasibility and acceptability.

Methods Hospital2Home was trialled at a specialist centre using a Phase II fast-track randomised controlled trial with qualitative interviews. The primary outcome for effect was mean change from baseline of Palliative Care Outcome Scale (POS) (a measure of symptoms and concerns) at 4 weeks. Secondary outcomes included symptom control, quality of life, consent and recruitment rates and percentage of patients in the fast-track group receiving case conferences within 14 days.

Results 53 patients were recruited (26 fast-track, 27 controls). Mean (SD) POS scores at 4 weeks were -5.7 (7.5) fast-track vs -0.4 (8.0) control, (mean change difference between the two arms was -5.3 (95% CI -9.8 to -0.7) independent t test $p=0.02$); effect size (95% CI) -0.7 (-1.2 to -0.1). The secondary outcomes of quality of life, anxiety and depression were superior in the fast-track arm, and none were worse. Qualitative findings corroborate these data. Recruitment was successful and 53/67 (79%) of eligible patients consented. 6/25 (24%) had case conferences within 14 days.

Conclusions Community case conferences improve palliative symptoms and quality of life after 4 weeks. Hospital2Home for the most part is both feasible and acceptable. It now requires further testing in multicentre trials.

Trial registration number NCT01450644

INTRODUCTION

Patients with idiopathic fibrotic lung diseases include a large patient subgroup with idiopathic pulmonary fibrosis (IPF), or with alternative diagnoses but an IPF-like outcome.¹ These patients experience substantial unmet symptom and psychosocial concerns that profoundly impact on patients'

Key messages

What is the key question?

► Could a palliative case conference intervention improve palliative care concerns and be feasible in advanced fibrotic interstitial lung disease (ILD)?

What is the bottom line?

► The case conference intervention may improve patients' and carers' palliative care concerns while being feasible and acceptable.

Why read on?

► People living with advanced fibrotic ILD experience high levels of unmet palliative care concerns and this work shows that evidence based palliative interventions such as the case conference can be developed and robustly evaluated to improve and direct care.

and carers' lives.²⁻⁴ In addition, poor communication and coordination of care, with little or no discussion surrounding important end-of-life preferences has been reported.⁴

Recent UK Government legislation promotes better integration of care to improve patient experience and outcomes, providing better continuity of individualised care at the end of life.^{5,6} Targeted organisation of care, improved communication and cooperation between disciplines across multiple healthcare settings is required to enable appropriate delivery of palliative care.⁷ Case conferencing at the interface between primary and specialist care may deliver individualised holistic care while addressing important unmet palliative care concerns.⁸⁻¹⁰ Research into case conferences in the non-malignant respiratory setting or centred on the patients' and carers' concerns are absent. In addition, there is a paucity of research developing complex interventions among those with fibrotic lung disease aimed at improving their symptoms and quality of life.¹¹

We conducted a phase II feasibility trial of a case conference intervention (Hospital2Home) to obtain

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preliminary information in what ways Hospital2Home influences the palliative care concerns of patients with advanced fibrotic interstitial lung disease (ILD) and their carers, and to evaluate the feasibility and acceptability of the intervention in this group.

METHODS

Study design

A fast-track (wait list) randomised controlled trial with embedded qualitative interviews were conducted as part of a larger project developing and evaluating Hospital2Home using the Medical Research Council's guidance for developing and evaluating complex interventions.¹² After consent and baseline interview, patients were randomised to fast-track or waiting list groups. For fast-track patients, a Hospital2Home nurse organised a case conference as soon as possible. Waiting list patients were referred for the case conference 4 weeks after randomisation. During the course of the trial, it became apparent that it was extremely difficult to get the case conference for those patients who were randomised to the fast-track group organised within 1 week and sometimes the waiting list group's case conference at exactly 4 weeks. An amendment allowed flexibility in the time points of the case conferences and the assessments. Treatment allocation (fast-track/waiting list group) was by computer generated random permuted blocks (by the Institute of Cancer Research) with stratification dependent on severity of patient Palliative Care Outcome Scale (POS) at baseline (patients with a POS score ≥ 28 were classed as severe).

Subjects

Patients with a clinical diagnosis of advanced idiopathic fibrotic lung disease (IPF by American Thoracic Society/European Respiratory Society criteria¹³ or fibrotic non-specific interstitial pneumonia) were recruited from the inpatient and outpatient settings in a specialist ILD centre (Royal Brompton Hospital, London). Patients included were considered to have end stage disease as judged by either high resolution CT or composite physiologic index scores. Total disease on CT was categorised as limited ($<40\%$), extensive ($>60\%$) or indeterminate ($40\text{--}60\%$). The proportion of honeycombing was recorded as limited ($<15\%$), extensive ($>35\%$) or indeterminate ($15\text{--}35\%$). Disease was classed as extensive if (1) Extensive disease ($>60\%$) or honeycombing ($>35\%$) on CT or (2) Composite Physiological Index >50 . Previous work done by Wells *et al*¹⁴ has shown a separation in survival between limited ($n=36$) and extensive ($n=100$) disease using this classification (HR=5.2 (CI 3.3 to 8.1) $p<0.0005$); the latter group (extensive disease) had a 10% survival at 2 years. A subsequent amendment allowed recruitment of patients considered to have end-stage disease clinically (based on clinical status, oxygen requirements and, in some cases, the presence of severe pulmonary hypertension) who were too unwell to complete pulmonary function tests.

To be included patients and carers had to be >18 years old, possess sufficient mental capacity and be able to complete questionnaires in English. Where possible, patient and carer dyads were recruited.

Intervention

All patients received best standard care throughout the study: Patients remained under ILD specialist care for the full duration of the study. This included receiving input from ILD physicians, ILD clinical nurse specialist, occupational therapist, physiotherapist and oxygen assessment and treatment services. In addition, all patients were able to access inpatient ILD treatment as needed. Referrals to community health professionals (as deemed

necessary by the ILD team) continued throughout the study. These could include referrals to community nursing (such as community matron or district nurses), respiratory services and community palliative care teams. The Hospital2Home intervention was delivered alongside best standard care (box 1). The fast-track group received the intervention after 1 week, the waiting list group after 4 weeks.

Primary outcome

The primary outcome was POS.¹⁵ POS was developed for patients with advanced cancer and includes aspects about pain and symptom control, patient and family psychosocial needs, and communication and information needs.¹⁵ The POS contains eight questions on anxiety, patient and informal caregiver concerns, and practical needs, each rated 0–4. The overall profile score is the sum of the scores from each of the 10 questions and can range from 0 to 40. Symptoms identified in preliminary work were added to question 2- 'Over the past 3 days, have other symptoms eg. having a cough, shortness of breath, fatigue or insomnia been affecting how you feel?'. This adapted POS was used to provide an assessment of change in palliative care needs (including symptom control).

Secondary outcomes

Secondary outcomes included changes in symptom control and quality of life measures (table 1). Details of each secondary measure can be located online in online supplementary appendix 1

Primary and secondary outcome data were collected by postal questionnaire at baseline in both groups. Subsequent time points were 4 weeks and 8 weeks after receiving the intervention in the fast-track group and just before receiving the intervention and 4 weeks after receiving the intervention in the waiting list group. Demographic information was also recorded. Qualitative interviews were conducted after completion of the trial. The topic guide used is depicted in figure 1.

Feasibility and acceptability

A priori criteria for trial feasibility were:

- ▶ Consent rate of at least 25%;
- ▶ Recruitment of 52 patients;
- ▶ 80% of patients in the fast-track group received their case conference within 14 days of randomisation.

The qualitative interviews were used in the post-trial evaluation to assess acceptability.

Sample size, randomisation and data analysis

Fifty-two patients were needed to enable estimation of change in POS between baseline and 4 weeks with accurate precision (assuming a SD of 2, a 95% CI for the difference between the fast-track and waiting list groups would be 2.2 units wide, ie, mean difference ± 1.1 units). Anticipated recruitment for qualitative work was 15 (5 patients, 5 carers and 5 health professionals).

We planned an intention-to-treat analysis. The differences in the change in POS scores (baseline to 4 weeks) between the fast-track and waiting list groups were compared using an Independent sample t test. For all secondary outcome measures descriptive methods were used to report the results in the groups using mean change scores with SD from baseline to week 4 and effect size at week 4. Only patients with week 4 data were included in change analysis. All quantitative data were analysed using Statistical Package for the Social Sciences (Version 21, IBM, Chicago, Illinois, USA).

Box 1 Hospital2Home intervention

Aims and rationale

The intervention aimed to provide a quality comprehensive palliative care assessment and streamlining of transfer of data between specialist and community settings improving coordination of care and communication while codifying responsibility for the patient, carer and health professionals. In the UK, a case conference model of care (Hospital2Home) has been used in patients with cancer in the acute oncology setting. The Hospital2Home model of care is unique as it has the advantages of a case conference (multiprofessional and holistic) and a care plan (care individualised to each patient and carer). The fibrotic interstitial lung disease Hospital2Home model was developed using Medical Research Council guidance and informed through a systematic review¹¹ and qualitative interviews.^{3 4}

Personnel

Provider: A palliative care specialist nurse delivered the intervention. The nurse had received training on delivery of the intervention from specialist nurses delivering the cancer Hospital2Home intervention.

Supervision: Clinical supervision was provided to assist in identifying and advising on strategies to address problems compromising effective management of the palliative care concerns of these patients and carers. The supervisors met with the nurse approximately weekly and provided additional telephone support as needed.

Attendees: The patient, their carer, Hospital2Home nurse, general practitioner, community matron/district nurse, respiratory nurse and community palliative care nurse (and any other health or social care professional involved in their care or identified as important by the patient) were invited to attend. All patients in the waiting list group who received the case conference had a carer who was present at the case conference. However only 19/25 patients in the fast-track group had carers and only 18 of these attended the case conference. There was consistent representation from community nursing and palliative care teams. However, less than 50% of general practitioners attended the case conferences.

Format

Setting: Case conferences were conducted in the community at a place chosen by the patient (all patients chose their home) Mean (SD) time in minutes taken to organise the case conference for fast-track group 204 (78) range 60–360 and for waiting list group 219 (86) range 60–390.

Schedule and duration: 25 patients in the fast-track group and 24 patients in the waiting list group received the case conference. The Hospital2Home nurse contacted patients after randomisation. For patients in the fast-track group where possible, the case conference was organised within 1 week (6/25 (24%) had case conference within 14 days, median 23 days, range 12–51). For patients in the waiting list group, this was organised for 4 weeks time (median 40 days, range 7–100). The median length of case conference was 90 min in both groups with a range of 60–120 min in the fast-track group and 60–150 min in the waiting list group. The Hospital2Home nurse followed up the case conferences in each group with the patient/carers via telephone at 2-week, 1 month and 2-month intervals. Patients and carers were also able to contact the nurse directly as needed for the length of the study. Contacts in addition to scheduled follow-up were mean (SD) 49 (78) min, range 0–300 min for the fast-track group and 35 (48) min, range 0–120 min for the waiting list group.

Content

Prior to the case conference, the Hospital2Home nurse telephoned the patient and carer to identify what their current palliative care concerns were and what they hoped to achieve from the case conference. This included identifying whether patients wished to discuss the sensitive matter of disease progression and planning for the future. During the case conference, which was led by the Hospital2Home nurse, current and anticipated care palliative care concerns were discussed. This included physical, psychological, social and spiritual concerns. In addition, where appropriate, end-of-life preferences were discussed. Preferred place of care—where the patient wished to be cared for in the last few weeks of life was discussed in 17 (68%) of fast-track and 23 (96%) of waiting list case conferences. For 13 (52%) of the fast-track group and 23 (96%) of the waiting list group this was home. Preferred place of death—where the patient wished to die was discussed at 11 (28%) of fast-track and 10 (42%) of waiting list case conferences. Reasons for non-discussion for preferred place of care and death were patient choice.

An action plan was agreed upon for each concern discussed at the case conference and a responsible healthcare professional allocated for each item. Following the case conference the Hospital2Home nurse, with contact details of each health professional, drafted an individualised care plan. The individualised care plan was then communicated to the patient and carer, the ILD specialist team, the general practitioner, all attendees at the case conference and any other health professional identified by the patient as involved in their care. The Hospital2Home nurse would check with the patient/carers at the follow-up phone calls that all action points on the care plan had been completed by the allocated health professional. The Hospital2Home nurse aimed to resolve any issues by liaising with the relevant community health professionals.

Delivery

Delivery methods: A collaborative problem solving approach was used whereby the patient and health professionals set agreed goals and jointly developed strategies to achieve them (with advice from the supervisors as needed).

Standardisation: Pro forma were used to standardise delivery and general content of the case conference and follow-up phone calls and to document issues arising from individual discussions, agreed goals, and difficulties and points for action or discussion at supervisory meetings. Symptom control management was guided by evidence based guidelines developed during preliminary work (available on request from corresponding author).

All qualitative interviews were digitally recorded and transferred verbatim onto a secure transcription database. Analysis was conducted using a constant comparison approach²³ within

Framework analysis as described by Ritchie and Spencer.²⁴ Qualitative analysis was facilitated by NVivo V.9. Efforts to maximise analytical rigour included dual coding of a sample

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Table 1 Outcome measures used

Baseline characteristic/ outcome	Instrument/measure
Patient	
Patient palliative care needs	Palliative Care Outcome Scale ¹⁵ with additional questions for breathlessness, cough, fatigue, insomnia (to be completed by patient and carer)
Patient breathlessness at best/worst	D12 scale ¹⁶
Patient quality of life	Kings Brief Interstitial Lung Disease questionnaire ¹⁷ and SGRQ ¹⁸ *
Patient functional ability	Medical Research Council breathlessness scale ¹⁹
Patient anxiety	Hospital Anxiety and Depression Scale ²⁰
Patient use of other services	Service use questions
Preferred place of care and death	
Carer	
Carer quality of life	Caregiver Quality of Life Index ²¹
Carer anxiety	Hospital Anxiety and Depression scale ²⁰
Carer's assessment of patient's use of services	Service use questions
Carer burden	Zarit Burden Inventory ²²

*After completion of a background systematic review,¹¹ it was decided to use SGRQ instead of the McGill Quality of Life questionnaire to enable comparison of outcomes with a number of other ILD studies. This amendment was made after recruitment and completion of the first patient in the trial.
ILD, interstitial lung disease; SGRQ, St Georges Respiratory Questionnaire.

selection of the interview transcripts and attention of deviant or non-confirmatory cases.

RESULTS

Patients were recruited October 2011–October 2013 and followed up until December 2013 (when the final patients recruited had completed 8 weeks in the trial) (figure 2).

Baseline measures

Baseline demographic and clinical characteristics for patients and carers are presented in table 2.

All analyses were by originally assigned groups.

Primary end point

There was a significantly greater reduction in total POS between baseline and week 4 for the fast-track group than in the waiting list group; mean change (SD) -5.7 (7.5) vs -0.4 (8.0), respectively. The mean change difference between the two arms was -5.3 (95% CI -9.8 to -0.7) independent t test $p=0.02$; effect size (95% CI) of -0.7 (-1.2 to -0.1) (figure 3).

Secondary outcomes**Patient**

For the fast-track group, initial improvements in POS score, King's Brief Interstitial Lung Disease (KBILD) questionnaire,

- What do you feel are the most important aspects of Hospital2Home? Prompts: evidence based guidelines, codifying responsibility, multi-professional working, crisis management, advance care planning
- What have you found particularly helpful? Prompts: evidence based guidelines, codifying responsibility, multi-professional working, crisis management, advance care planning
- Is there anything about the intervention that you found unhelpful?
- What if any improvements would you like to see in the model of care?

Figure 1 Topic guide used for qualitative interviews.

and Hospital Anxiety and Depression scale (HADS) scores at 4 weeks were all sustained or continued to improve further by week 8 (see table 3). In contrast these indices did not significantly improve by week 4 for the waiting list group (and actually worsened for POS and KBILD questionnaire scores) but showed significant improvement once the intervention was delivered (ie, comparison weeks 4–8). There was also improvement in impact and total scores for St Georges Respiratory Questionnaire (SGRQ) scores in the fast-track group compared with the waiting list group. SGRQ scores for symptoms, impact and total scores also improved in the waiting list group once the intervention was delivered.

Positive effects were identified for patient HADS scores at week 4. This effect was sustained in the fast-track group with continued improvement. There was also improvement in the waiting list group for anxiety, depression, and total scores after the intervention was delivered.

There was no improvement in D12 scores in the fast-track group but there was an improvement in D12 scores between week 4 and week 8 in the waiting list group. There was no change in the Medical Research Council scores across both groups over time.

Carer

There was no significant difference in POS between the fast-track and waiting lists groups at week 4. However, there was a marked improvement in waiting list scores between week 4 and week 8 (18.0 (8.4) vs 13.7 (6.3)), respectively. Zarit Burden Inventory score and Carer Quality of Life Cancer burden, disruptiveness, financial and total scores followed a similar pattern with no effect of the intervention at week 4. This was followed by improvement in scores between week 4 and week 8 in the waiting list group.

There were borderline effect sizes of the intervention on depression and total HADS scores (-0.7 (-1.3 to 0.0) and -0.7 (-1.3 to 0.0), respectively). This was followed by improvement between week 4 and week 8 scores for the waiting list group for anxiety (11.7 (5.6) vs 9.8 (4.6)), depression (9.6 (4.9) vs 7.2 (3.9)) and total score (21.3 (9.9) vs 17.0 (8.2)), respectively.

Data related to study

As of study close on 31 December 2013, a greater number of waiting list patients (13 (54%)) had died than fast-track (8 (32%)). Preferred Place of Care and Preferred Place of Death were less likely to be achieved for patients who died in the waiting list group; Preferred Place of Care: fast-track (FT 8) (100%) versus waiting list (WL 11 (84%)), Preferred Place of Death: FT 7 (88%) versus WL 10 (77%). More patients died at home in the fast-track group; FT 5 (62%) versus WL 5 (38%) and in hospital in the waiting list group; FT 1 (12%) versus WL 5 (38%). All three patients who died before being able to receive the case conference were in the waiting list group and all died in hospital.

Qualitative findings

Online supplementary appendix 2 shows the qualitative participants' characteristics. Key quotes are presented in table 4 and the full qualitative findings can be found in online supplementary appendix 2.

DISCUSSION

This fast-track randomised controlled trial of a case conference intervention in patients with advanced fibrotic ILD and carers identified an improvement in symptom control and quality of

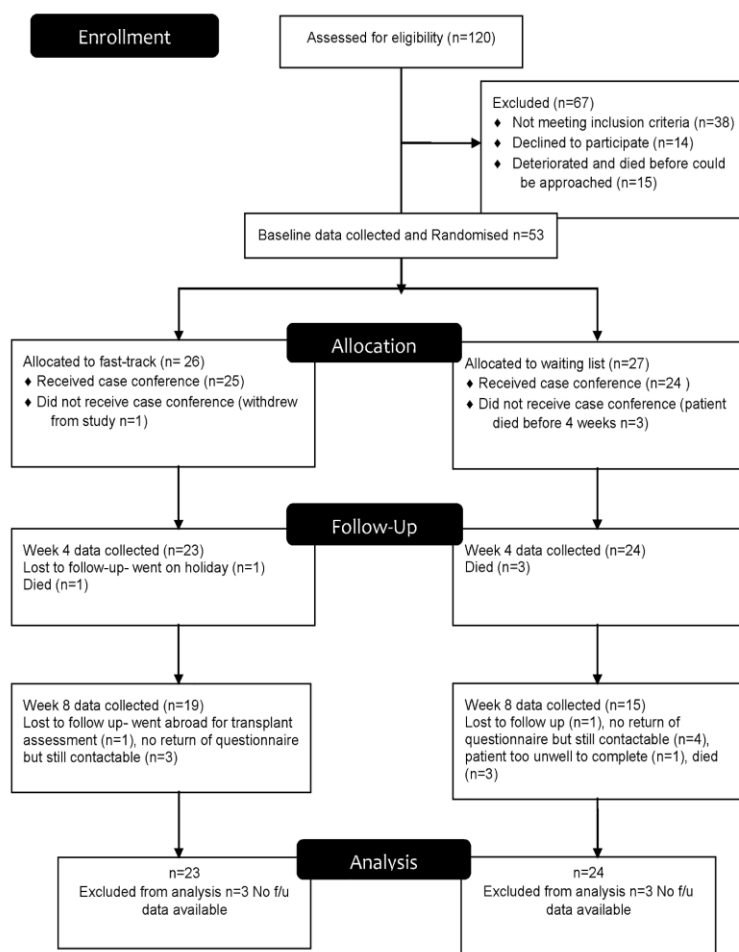


Figure 2 CONSORT diagram showing flow of patients through the study.

life. Of note, there was no worsening of any outcome after receiving the intervention. This suggests that no harm and potentially a prevention of deterioration may have occurred. Mean change difference scores in POS in the fast-track group were 5.7 points at 4 weeks, sustained at 8 weeks. For POS, a variation of one point in individual items is linked to clinical meaningful change.¹⁵ There was also a promising large effect size. Similar improvements in the waiting list POS once they received the intervention suggest that the intervention may improve the palliative care concerns of these patients. Use of evidence based guidelines and a comprehensive palliative care assessment at the case conference, ongoing palliative care involvement and/or added time with care providers may have contributed to this.

Baseline scores showed that patients were living with poor quality of life. Improvements were observed in the KBILD and SGRQ impact and total scores at week 4 in the fast-track group. The improvement in the waiting list SGRQ impact and total scores were marked between week 4 and week 8 where both domains showed improvement greater than the Minimal Important Clinical Difference for IPF. Improvements were also identified in anxiety and depression scores. Of note, baseline

mean patient anxiety and depression scores and mean carer anxiety scores in both groups were borderline abnormal or abnormal. Importantly, the waiting list group showed deterioration for all anxiety and depression scores in the patients and carers during the 4 week wait. However, this improved after receiving the intervention. Clinically meaningful improvements in HADs scores of patients and their carers (the Minimal Important Clinical Difference in COPD is 1.5²⁵) were identified. These improvements find correspondence with the qualitative interviews. Before the case conference, patients and carers stated they had very little knowledge of support they were entitled to and were suffering alone. Through the case conference, patients and carers had access to specialist community palliative care services that routinely support patients' and carers' holistic palliative care concerns. Patients and carers felt that this reduced anxiety. Moreover they were grateful for the clear crisis management strategy provided through the individualised care plan. Patients and carers interviewed valued the case conference itself as they felt that it 'laid everything on the table' and importantly addressed concerns and anxieties that had been playing on patients' and carers' minds. This supports findings by Lindell

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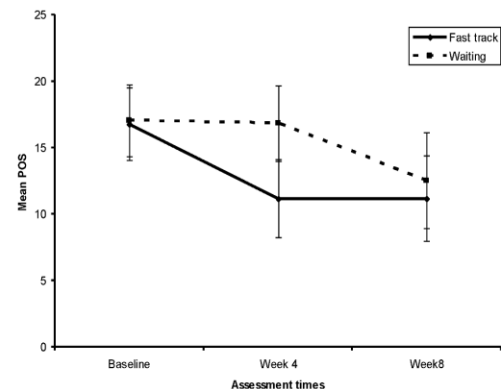
Table 2 Summary table of baseline demographic and clinical data

Patients	Fast-track N=26	Waiting list N=27
Age (years)	67.1 (10.9)	70.6 (10.3)
Male	20 (77%)	18 (67%)
Ethnicity		
White UK	21 (81%)	20 (74%)
Black or Black British	1 (4%)	2 (8%)
Asian or Asian British	4 (15%)	5 (18%)
Disease		
IPF	22 (85%)	22 (82%)
NSIP	4 (15%)	5 (18%)
Diagnostic biopsy		
Surgical	8 (31%)	6 (22%)
Not carried out	18 (69%)	21 (78%)
% predicted TLCO		
Mean (SD)	25 (10.7)	23 (5.8)
Not carried out	4 (15%)	4 (15%)
Extent of disease on CT		
Limited (<40%)	3 (12%)	3 (11%)
Indeterminate (40–60%)	9 (35%)	14 (52%)
Extensive (>60%)	14 (54%)	10 (37%)
Extent of honeycombing on CT		
Limited (<15%)	10 (38%)	11 (41%)
Indeterminate (15–35%)	11 (42%)	10 (37%)
Extensive (>35%)	5 (19%)	6 (22%)
Composite Physiological Index		
>50	19 (73%)	27 (100%)
Mean (SD)	66.5 (4.0)	64.8 (3.6)
Not carried out	7 (27%)*	0
Using oxygen		
Yes	20 (77%)	23 (85%)
Litres/h used	3 (1.4)	3 (1.1)
Usage in 24 h	19 (6.6)	21 (5.3)
Comorbidities		
Yes	17 (65%)	13 (48%)
Heart failure	1	0
COPD	4	1
Pulmonary embolism	1	0
TB	0	0
Cancer	1	1
Diabetes	5	4
Other	13	10
Carers	N=19	N=26
Age	61.3 (14.0)	60.3 (13.1)
Male	6 (32%)	6 (23%)
Ethnicity		
White UK	17 (90%)	18 (69%)
Black or Black British	1 (5%)	2 (8%)
Asian or Asian British	1 (5%)	6 (23%)

Data are means (SD) or numbers (%).

*Three patients were recruited who had end-stage disease clinically, did not have extensive disease or honeycombing on CT and were too unwell to complete lung function tests.

IPF, idiopathic pulmonary fibrosis; NSIP, Non-specific interstitial pneumonia; TLCO, carbon monoxide transfer factor.

**Figure 3** Line diagram showing change in mean Palliative Care Outcome Scale (POS) with 95% CIs over time in the two groups.

Hospital2Home aimed to facilitate early discussion about disease progression, to improve communication and address end-of-life planning needs. Not all patients wanted to talk about advance care planning decisions such as preferred place of care and preferred place of death. This was similarly identified by Abernethy *et al*¹⁰ where prognosis, end-of-life issues, and previous experiences of death were rarely discussed at the case conference for patients with cancer. For those patients in this trial who did discuss advance care planning, even though it could initially be distressing for relatives, it was seen as incredibly useful. For some patients, the case conference provided them with permission to conduct these important conversations. Interestingly, patients who did not want to discuss advance care planning at the case conference then went on to have subsequent discussions with their community health professionals. This may have been precipitated by those initial discussions by the Hospital2Home nurse and the development of relationships with the community palliative care team after the case conference. For patients who wished to discuss preferred place of death, no patients reported hospital as their preference. The actual place of death for patients having received the case conference was hospital in only 28% of patients. This is much less than observed in a retrospective case note review² where 76% of patients with advanced fibrotic ILD attending two acute hospitals died in hospital. Interestingly, the three patients who died in the waiting list group before receiving the intervention, died in hospital. Patients with IPF experience increased healthcare resource utilisation, and direct medical costs.²⁷ This is important at the end of life. It is possible that the case conference, through documenting end-of-life preferences, establishing links in the community setting, and preventing crisis admissions enabled patients not to die in hospital. The economic impact of this requires further investigation.

The fast-track study design worked effectively and is likely to be an influencing factor as to why consent and recruitment rates were met as all patients received the intervention. However, only 24% of the fast-track group received the case conference within the a priori 14-day allotted time frame. Health professionals were often unable to schedule a case conference within a week's notice. This has been found previously; Abernethy *et al*¹⁰ observed that only 38/167 case conferences in their trial were held within 28 days. When considering the waiting list period, 4 weeks was chosen as this was considered long enough to identify an effect of the intervention on the primary

et al who evaluated an interventional disease management programme in IPF and Higginson *et al*'s²⁶ recent trial of a breathlessness intervention service among 105 patients with refractory breathlessness (including patients with ILD). Both observed improvements in psychological symptoms.

Table 3 Outcome measure data: outcome data for completed (fully or partially) measures have been presented

	Fast track				Waiting list				
	Baseline (mean (SD) or n (%))	4 weeks (mean (SD) or n (%))	Change score Mean (SD)	8 week (mean (SD) or n (%))	Baseline (mean (SD) or n (%))	4 weeks (mean (SD) or n (%))	Change score Mean (SD)	8 week (mean (SD) or n (%))	Effect size (95% CI) at 4 weeks
Primary end point	N=26	N=23			N=27	N=24			
POS	16.8 (5.6)	11.2 (7.9)	-5.7 (7.5)		17.0 (6.3)	16.8 (8.9)	-0.4 (8.0)		-0.7 (-1.2 to -0.1)
The mean change difference between the two arms was -5.3 (95% CI: -9.8 to -0.7) Independent t test p=0.02									
Secondary outcomes									
Patients									
POS				N=19 11.2 (7.3)				N=15 12.5 (6.6)	
D12	N=25* 22.8 (8.7)	N=22* 21.6 (10.1)	-0.8 (7.2)	N=19 20.4 (9.8)	N=27 25.9 (8.2)	N=24 25.0 (10.7)	-0.6 (21.3)	N=15 21.3 (10.5)	-0.3 (-0.9 to 0.3)
KBILD†	N=26 35.8 (13.0)	N=23 40.0 (16.2)	3.5 (11.0)	N=19 43.2 (18.4)	N=27 32.3 (12.9)	N=24 30.3 (16.2)	-2.6 (21.3)	N=15 34.9 (18.0)	0.6 (0.0 to 1.2)
SGRQ	N=25‡ 62.2 (17.7)	N=22‡ 62.0 (20.5)	1.4 (16.5)	N=18‡ 52 (20.1)	N=26§ 66.3 (24.5)	N=24 65.8 (23.0)	-2.0 (23.7)	N=15 60.2 (23.8)	-0.2 (-0.8 to 0.4)
Symptoms	88.9 (9.7)	85.3 (17.6)	-3.1 (13.6)	87.1 (10.7)	93.7 (5.0)	92.4 (7.8)	-1.6 (6.8)	91.4 (5.2)	-0.5 (-1.1 to 0.1)
Activity	61.6 (18.0)	56.3 (20.3)	-4.0 (19.7)	57.4 (20.8)	71.4 (12.8)	74.8 (14.9)	2.8 (13.3)	62.3 (13.5)	-1.0 (-1.6 to -0.4)
Impact	70.0 (13.0)	66.0 (16.4)	-2.8(14.9)	65.7 (14.7)	76.8 (10.1)	78.6 (11.8)	0.7 (10.5)	70.8 (10.8)	-0.9 (-1.5 to -0.3)
Total	N=26 Median 4	N=23 4		N=19 4	N=27 5	N=24 5		N=15 4	
MRC	4-5	4-5		4-5	4-5	4-5		4-5	
IQR (25-75)	N=26 9.6 (4.6)	N=23 8.1 (4.1)	-1.7 (3.3)	N=19 7.1 (4.6)	N=27 9.7 (5.7)	N=24 10.8 (5.5)	1.2 (4.8)	N=15 7.9 (5.5)	-0.6 (-1.1 to 0.0)
HADs	9.0 (3.1)	9.4 (3.0)	0.3 (3.2)	8.3 (3.7)	11.0 (4.7)	12.3 (4.8)	1.5 (4.12)	9.3 (4.5)	-0.7 (-1.3 to -0.1)
Anxiety	18.6 (6.4)	17.5 (6.3)	-1.4 (5.0)	15.4 (7.7)	20.7 (9.0)	23.0 (9.7)	2.8 (8.1)	17.2 (9.4)	-0.7 (-1.2 to -0.1)
Depression									
Total score									
Carers									
POS	N=19 17.8 (6.5)	N=15 14.7 (6.5)	-2.9 (5.8)	N=13 16.1 (6.9)	N=26 18.5 (6.2)	N=22 18.0 (8.4)	-0.7 (9.6)	N=15 13.7 (6.3)	-0.4 (-1.1 to 0.2)
ZBI	N=19 22.2 (15.2)	N=16 22.3 (15.3)	0.1 (0.2)	N=13 26.2 (13.4)	N=26 32.2 (11.7)	N=23 31.7 (17.3)	-0.1(0.3)	N=16 25.4 (13.4)	-0.6 (-1.2 to 0.1)
HADs	N=19 9.3 (4.3)	N=16 8.8 (4.8)	-0.5 (4.8)	N=13 9.2 (3.7)	N=26 11.0 (5.9)	N=23 11.7 (5.6)	0.6 (5.3)	N=16 9.8 (4.6)	-0.6 (-1.2 to 0.1)
Anxiety	7.0 (4.9)	6.4 (4.1)	-0.3 (3.5)	7.0 (4.2)	8.7 (5.0)	9.6 (4.9)	1.0 (4.6)	7.2 (3.9)	-0.7 (-1.3 to 0.0)
Depression	16.3 (8.7)	15.2 (8.3)	-0.8 (8.0)	16.2 (7.4)	19.7 (10.4)	21.3 (9.9)	1.7 (8.7)	17.0 (8.2)	-0.7 (-1.3 to 0.0)
Total score	N=18 21.9 (8.3)	N=15 21.5 (7.1)	-0.6 (6.9)	N=13 20.2 (5.7)	N=25 25.2 (8.3)	N=21 25.2 (8.5)	-0.2 (8.0)	N=13 22.1 (9.2)	-0.5 (-1.1 to 0.2)
CQLC†	7.8 (6.0)	7.1 (6.9)	-0.6 (4.3)	7.7 (4.8)	9.6 (5.4)	9.3 (5.5)	0.0 (4.9)	7.6 (5.9)	-0.4 (-1.0 to 0.3)
Burden									

Continued

All analyses conducted by originally assigned groups.
Lower scores on the SGRO and higher scores on the KBILD indicate a better quality of life.
*One patient had >three items missing on the D12 questionnaire and was therefore excluded as per author's instructions.
†Increase in scores indicates improvement.
‡One patient completed McGill quality of life not SGRO.
§One patient removed as >six items missing on activity SGRO.
¶CQLC, cancer quality of life cancer; HADS, Hospital Anxiety and Depression Scale; KBILD, King's Brief Interstitial Lung Disease questionnaire; MRC, Medical Research Council Scale; SGRO, St George's Respiratory Questionnaire; ZBI, Zarit Burden Inventory.

There are a number of limitations to this trial. POS has not been validated in ILD, however, nor have other holistic palliative care measures. This phase II trial was not adequately powered to identify efficacy, therefore results must be interpreted with caution. Despite this the trend towards positive differences between groups was observed and strongly suggests a further adequately powered study that is informed by the learning from this study. Referrals to community services for the waiting list group were made at randomisation and beyond the control of the study, a few community services contacted

Table 4 Presentation of qualitative findings (all names have been changed to ensure confidentiality)

Theme	Participant	Example quote
Support in the community	Ann, 72-year-old wife of Stephen who had advanced NSIP	"I was bit nervous before hand you didn't have anyone to turn to really.....we have one son in xxxx but he's far away and (2) I have a sister in xxxx which phones me up every day but [coughs] otherwise that's I felt alone::e" and how do you feel now?" (SB) "I feel better..... 'cause I have all the phone numbers and people phone me up..."
Individual care plans and practical problems addressed	Community palliative care CNS	"[the H2H CNS] contacted us afterwards to check everything we had said we were going to do we'd done which we had erm::: and we had her number to be able to contact if he had any problems as well so::: erm it went all quite smoothly really..."
Coordination of care and efficiency	GP	"if it wasn't for this (2) I can see a completely different scenario where this guy would be lost in the communityhe::: would be trying to find out who::: the respiratory nurse is [laughs] trying to get out who's the oxygen supplier trying to find out from his GP which one's going to be in charge of his care in the general practice which one's going to be helping him with his symptoms (1) you know it it would have become a hug:::e hassle and I don't think he::: realises how lucky he is actually to be part of this trial (2) because everything's there for him (2) there's no other issue..."
Crisis management	Peter, 63-year-old with advanced IPF	"and now I've got all erm (2) they as I say they phone and I've got er a whole list of numbers that I can phone any time day or night erm if I need to, you know....oh yes yeah and (1) and (2) as I say I've got erm the telephone numbers... of people that I can phone erm 24 seven which is ideal I mean before that erm the most I could do was dial 999"
Palliative care, psychological support	Ted, 55-year-old patient with advanced IPF	"I must say to everybody (2) definitely it is it's (2) I don't know how long I've got left but (2) whatever time I've got left (3) this palliative care is going to make that time better for me and it's better and if it's better for me it's better (2) for us as a family....I've been telling everybody (2) how important (3) you know I just wish I could get GPs in to buy into the (2) palliative care cause its makes such a difference (2) made such a difference to me..... I have weeks when (2) er like last week I wanted to talk about (3) you know (2) my illness and stuff...and they're there then (2) for me to be able to tap into.. which I am happy for because (3) when you're in in my my sort of position when you know your life limited (1) is your life is limited often at home (3) you tend you live a lie say to people you live a lie I think because say how do you feel you just say I feel fine but because you don't want to be worrying people all the time but (1) when you've got a palliative care team round you you can get that out of your system which is something we didn't have for the first 18 months two years of this disease"
Symptom control	ILD Consultant	"We would star:::t er symptom control in hospital whether that was a little bit of Oramor:::ph or lorazep:::am and then it was really we wouldn't often see the patient for another 3 or 4 months time and it was then back to the GPs han:::ds to sort of titrate and change that as needed um and it didn't always go successfully the things weren't re-prescrib:::ed or wrong doses were given but knowing that er (1) you and your team are now doing that again we've had patients say that it's been very useful for them to have sort of continuity of care and someone taking overall view of that...."
Empowering HP	ILD CNS	"It's certainly enhanced my practice, um, certainly there's an huge (1) element of my job which is dealing with um the palliative care and end of life of patients, and I think, seeing how palliative care interact with patients and bring up (1) uncomfortable::: (2) subjects for us as healthcare professionals, certainly has enhanced my practice....We need to::: (1) understand that these aren't necessarily subjects that patients don't want to discuss...sometimes some of the anxiety around the issues can be discussing what the future is, discussing, (1) you know, having those uncomfortable conversations. I think, H2H has facilitated that, helped patients be more organised and think around what they're doing and also highlighted to us how to go about those conversations, and that those conversations are (1) ok to have."
Advance care planning	Leslie, 54-year-old wife of Ted who had advanced IPF	"For us it was a bit traumatic you know everything being coming to life that actually these things are happening I think you can go to hospital appointments and still sort of brush it aside that you know [laughs] erm (2) but once everybody was sat round the table and we talked about DNRs ...and erm (4) advanced directives and all this sort of stuff it did bring it home and it did get a little bit (3) upsetting but (3) I I still do believe that it was better at that point than when (1) somebody's actual laid on their bed and you think it could be any da:::y and (2) erm (1) you know I think you can deal with it better at that stage"

CNS, Clinical nurse specialist; DNR, Do not resuscitate; GP, General practitioner; H2H, Hospital2Home; HP, Health professional; ILD, interstitial lung disease; IPF, idiopathic pulmonary fibrosis; NSIP, Non-specific interstitial pneumonia.

patients and carers before the case conference. This coupled with the delay in delivering the case conference to the fast-track group may have affected comparison of the efficacy of the intervention at the primary end point of 4 weeks. However, these factors are likely to have underestimated rather than overestimated any effect. The high resolution computed tomography/composite physiologic index criteria for excluded patients were not recorded which may have provided valuable clinical information. The Hospital2Home intervention is a complex intervention with multiple different components. Attempts were made to standardise delivery as much as possible with pro

forma and evidence based guidelines. Despite this, there is likely to have been some variance in delivery. Due to constraints of the study, outcome measures were not collected after the 8 week mark. This may have provided valuable information of possible effects of the intervention over time.

CONCLUSION

Preliminary evidence from this trial reveals a positive effect on patients and carers of the Hospital2Home intervention on palliative care concerns, quality of life and anxiety and depression. In addition, the intervention managed uncertainty by facilitating

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early discussion about disease progression, improving communication and addressing end-of-life planning needs. The Hospital2Home intervention therefore appears to be feasible, acceptable and effective across a number of domains.

As this is a phase II study, any positive effects may be promising but would need to be further examined in a multicentre phase III study before conclusions about wider effectiveness may be drawn. However, the information obtained from this trial will allow sample size calculation in future studies. In addition, this study has provided valuable information about the patients and carers affected by advanced idiopathic fibrotic ILDs as well as the potential effects of the Hospital2Home intervention in this group.

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APPENDIX 1

Outcome measures used

The D12 scale is an overall score for breathlessness severity that incorporates seven physical items and five affective items.[1] Participants complete the D-12 in reference to their experience of breathlessness “these days” at baseline and follow-up. D-12 consists of 12 descriptor items on a scale of none (0), mild (1), moderate (2), or severe (3). Total scores from the D-12 range from 0 to 36, with higher scores corresponding to greater severity. It has not been validated in ILD.

The King’s Brief Interstitial lung disease is a 15 item questionnaire consisting of three domains (breathlessness and activities, chest symptoms and psychological).[2] It has been validated in all ILD disease groups including IPF. A higher score indicates a higher quality of life (QoL). Scores range from 0-100 with the minimal important difference of 8 units of the total score.[3]

The St George’s Respiratory questionnaire [4] is a 50 item instrument designed to measure impact on overall health, daily life, and perceived wellbeing in patients with obstructive airways disease. Part 1 has a symptoms component (frequency and severity) with a 1, 3 or 12 month recall (several scales); Part 2 has a activities component looking at activities that cause or are limited by breathlessness and an impact component looking at social functioning, psychological disturbances resulting from airways disease and referring to current state as the recall (dichotomous (true/false) except last question (4 point Likert scale)).[5] The MID for IPF in each of the SGRQ domains is Symptoms 8 units, Activity 5 units, -Impact 7 units and Total 7 units.[4] A lower score indicates a better quality of life. The generic SGRQ version has been validated in IPF.[4]

The Medical Research Council (MRC) dyspnoea scale (score range, 1-5, with higher scores indicating greater impairment) [6] is used to classify participants according to activity

limitation. The MRC scale comprises five statements that describe almost the entire range of respiratory disability from none (Grade 1) to almost incapacity (Grade 5). It is self-administered by asking subjects to choose a phrase that best describes their condition. The MRC breathlessness scale does not quantify breathlessness itself. Rather, it quantifies the disability associated with breathlessness by identifying that breathlessness occurs when it should not (Grades 1 and 2) or by quantifying the associated exercise limitation (Grades 3–5). It has not been validated in ILD patients.

The 14-item Hospital Anxiety and Depression Scale (HADS) is a widely used tool for assessing psychological distress.[7] The HADS comprises seven items that tap anxiety (score range, 0-21) and seven items that tap depression (score range, 0-21), with higher scores corresponding to greater distress. Scores of 0-7 are classed as normal, 8-10 borderline abnormal and 11-21 abnormal. The HADs may be completed by both patient and informal caregiver. The HADs has not been validated in IPF. The MID in COPD is 1.5.[8]

The Carer Quality of Life Cancer (CQOLC) measures four conceptual domains of QoL: physical functioning, emotional functioning, family functioning and social functioning.[9] The CQOLC consists of 35 items that have a five-point Likert format that range from 0 (not at all), 1 (a little bit), 2 (somewhat), 3 (quite a bit) and 4 (very much): ten items relate to burden, seven to disruptiveness, seven to positive adaptation, three to financial concerns and eight single items to additional factors (disruption of sleep, satisfaction with sexual functioning, day-to-day focus, mental strain, informed about illness, protection of patient, management of patient's pain and family interest in caregiving). The CQOLC scale is scored by adding up the score on each item to yield a total score for the instrument and scores can range from 0-140. For all items and domains that measure QoL, a higher score represents a better QoL.[9] There is no current tool to measure informal caregiver Qol in non-malignant respiratory disease. Therefore the CQOLC was used which has been validated in cancer patients.

The Zarit Burden Interview (ZBI) was developed to measure subjective burden among informal caregivers of adults with dementia.[10] Items were generated based on clinical experience with informal caregivers and prior studies resulting in a 22-item self-report inventory that examines burden associated with functional/behavioural impairments and the home care situation. The items are worded subjectively, focusing on the affective response of the informal caregiver.[11 12] Each question is scored on a 5 point Likert scale ranging from - never to nearly always present. Total scores range from 0 (low burden) to 88 (high burden). There is no validated tool to measure caregiver burden in ILD.

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APPENDIX 2- Table showing qualitative participants' characteristics (names have been changed to ensure confidentiality)

Study ID	Study name	Profession	Ethnicity	Age	Number of patients involved with who had H2H CC	Field notes (if any)
HP1		ILD Consultant	White other	37	18	
HP2		ILD CNS	White British	31	32	
HP3		Community Matron	Philipino	30	2	Involved in the care of 2 patients that died at home as planned. Although consented to interview, this subject was very hesitant to make any comments that might be perceived as negative.
HP4		Community Palliative Care Nurse	White British	31	1	
HP5		GP	Asian British	42	1	GP very keen to take part in interview and feedback his views. GP for 34 year old patient with IPF.
P1	Alfred		White British	64		Patient with advanced IPF (no carer) on transplant list. Patient admitted for trial of NIV. Happy to take part in interview.
P2	Michael		White British	63		Advanced IPF with no carer. Patient unhappy with the state of NHS. Interviewed at home.
P3	Peter		White British	63		Advanced IPF with carer. Interviewed on day unit. Patient wearing oxygen. Struggling at times with SOB
P4	Stephen		White British	81		Fibrotic NSIP. Patient interviewed at home. Wife also interviewed as carer. Both interviewed separately.
P5	Mary		White Irish	84		Patient (NSIP) interviewed at home- relatively well at time- daughter interviewed
C1	Ann		White British	72		Wife of P4- interviewed at home.
C2	Sue		White Irish	48		Daughter of P5. Interviewed alone.
C3	Rachel		Black Caribbean	47		Daughter of 75 year old patient with IPF (not interviewed). Sole carer for patient.
C4	Leslie		White British	54		Wife of Ted- patient 55 year old patient with IPF. They have a 23 year old son with cerebral palsy which Ted is the main carer for. Interviewed at home with husband present.
C5	Penny		White British	63		Wife of 67 year old patient with IPF. Interviewed alone. Patient not interviewed

Recruitment for the qualitative study was conducted between May 2013 and November 2013. 5 patients, 5 carers and 5 health professional participants were recruited. Health Professionals (HP) recruited were an ILD Consultant, ILD CNS, community matron, community palliative care nurse and a GP. The qualitative results will be discussed in the following themes: 1) *Support in the community* 2) *Individual care plans and practical problems addressed* 3) *Co-ordination of care and efficiency* 4) *Crisis management* 5) *Palliative Care and psychological support* 6) *Symptom control* 7) *Empowering HP* 8) *Advance care planning* 9) *Feasibility and acceptability of intervention*.

Examples of quotes have been used to illustrate themes. Names have been changed to ensure confidentiality.

Theme 1 Support in the community

Previous to the Case Conference (CC), both quantitative and qualitative data showed that patients and carers were poorly supported. Patients and carers interviewed received routine care from their primary care physician. However, no patient or patients looked after by carers had any other professional help. Importantly, as well as not receiving support from HP in the community, no patients or carer participants interviewed were aware of the services that were available to them. In addition, if the patient or carer participants needed help, they often relied on the specialist ILD centre. However, the distance to RBH often caused patient and carer participants concern. This was typified by Leslie, 54 year old wife of Ted who had advanced IPF:

“What was it like erm before you had the CC what sort of input and help were you getting?” (SB)

“nothing we weren’t getting anything not from (2) not locallyreally (2) anything we needed we had to either go to or phone London.....and it’s like so it’s a 2 hour [laughs] it’s a 2 hour round trip.....but (1) that was quite scary cause you sort of think you know it’s a long way away you know if we need (4) u:::m (1) so local support just wasn’t there.....” (Leslie, 54 year old wife of Ted who had advanced IPF).

Patient participants such as Stephen, a 81 year old patient with NSIP, had felt that prior to the CC they had not known what they were doing. Importantly, through the CC patient, carer and HP participants became more aware of the services that patients and carers were entitled to. All participants reported that through the CC, patients and carers received support from a variety of community HP. Patients and carers commented that they were regularly contacted by community HP to check that they were "okay". The community HP would not necessarily visit every week but would phone to touch base with the patient and carers. Patient and carer participants commented on how it was reassuring that someone was checking on them and that this made them feel "safe" and how they were grateful for all the help that they were now receiving.

"I think] I'm very lucky....I didn't think that help was there" (Mary, 84 year old with NSIP)

Carers felt happier to have access to a support network in the community. For example, carers such as Ann, 72 year old wife of Stephen who had advanced NSIP, reflected on how they had felt isolated and were required to muddle through before:

"I was bit nervous before hand you didn't have anyone to turn to really.....we have one son in xxxx but he's far away and (2) I have a sister in xxxx which phones me up every day but [coughs] otherwise that's I felt alon:::e" (Ann, 72 year old wife of Stephen who had advanced NSIP)

"and how do you feel now?" (SB)

"I feel better..... 'cause I have all the phone numbers and people phone me up...." (Ann, 72 year old wife of Stephen with advanced NSIP)

Patients like Peter (63y with advanced IPF) were grateful for having been involved in the study and receiving support which he felt he would not have got if it had not been for the CC. Touchingly, he reflected on those who were still not receiving support. He stated:

".....because before that [CC] erm well I say they they wouldn't have known about me anyway erm (3) but (2) its [coughs] for people that are maybe not coming her:::e erm they they can be sitting indoors erm with no no help and not

knowing where to get it which is a shame" (Peter, 63 year old with advanced IPF).

Theme 2 Individualised care plan and practical problems addressed

Through the CC, an individualised care plan specifically meeting the patients' and carers' palliative care needs was developed. Using the evidence based guidelines, symptom control issues were addressed. Specific action points were allocated to each HP codifying responsibility. After the CC, the H2H CNS contacted the patient and followed up with the HP to ensure tasks were completed. In addition, in the care plan patients and carers had the contact details of how to contact each of the HP directly if there were any issues. This process is illustrated by the Community Palliative Care CNS:

"[the H2H CNS] contacted us afterwards to check everything we had said we were going to do we'd done which we had erm::: and we had her number to be able to contact if he had any problems as well so::: erm it went all quite smoothly really..." (Community Palliative Care CNS)

Many patients and carers had practical problems that needed to be addressed. Both patients and carers expressed how quickly after the CC these practical issues were attended to especially as many patients had been waiting a long time for these issues to be addressed. Rachel (47 y), whose mother had not received any care prior to the CC, reflected on how after the CC things moved very quickly. She said:

"...the district nurse she was just making sure that erm mum is comfortable er:::m cause at the I think that was the time when they all came mum was suffering with bed sore:::s.....so that was erm (2) a problem and I mean (1) it was dealt with fantastically because erm (3) xxxxx (2) made sure that a bed (1) hospital bed was delivered within two three days..." (Rachel, 47 year old daughter of patient with advanced IPF)

The GP felt that as responsibility was codified and patients/carers had contact numbers for all HP on the care plan, HP were more likely to follow through on tasks.

Importantly, the individualised care plan holistically focussed on the needs of the patient, carer and where applicable, other family members. Patients and carers during the qualitative interviews reported how beneficial this was. Quantitative data also showed a significant change in patient POS (measuring holistic palliative care needs of the patient) score for the FT group at week 4 and the WL group at week 8. Leslie discussed how the CC allowed their concerns for their son (which were at the forefront of their minds and fundamental to improving their quality of life) to be addressed by the social worker attending the CC:

“our er::m (2) youngest son’s got cerebral palsy.. so erm after that meeting [CC] it was put in place for him to have erm (4) er counselling erm (3) and to explain to hi::m (2) erm what was happening... and so he has a better understanding now erm (2) because it’s difficult to know you know you need somebody really from the erm (2) special nee::ds to (2) to get through to them in in in the way that needs to be done rather than (1) so we had that put in place as well after the meeting [CC]” (Leslie, 54 year old wife of Ted who had advanced IPF).

Theme 3 Co-ordination of care and efficiency

Before the CC, patients and carers stated that there was a lack of co-ordination and efficiency in the care that was delivered. Stephen, a 81 year old patient with NSIP, expressed his frustrations with the lack of effectiveness of the health system:

“there was a lot of people didn’t know what to do with me a- quite I I suspect um I I can’t say for sure [deep intake of breath] and it seemed to be I’ve (1) been pushed from one to another or pushed round and round in circles I was taking a lot of er (1) tests (2) and they were all being sort of duplicated” (Stephen, a 81 year old patient with NSIP)

Post CC there appeared to be some improvement; Alfred, 64 year old patient with advanced NSIP and no carer felt that the CC allowed everyone to “sing from the same hymn sheet” improving efficiency of the care delivered. In addition if an admission did occur, the care plan gave clear

information about who was involved in the patient's ILD care. Carers such as Sue felt that having the care plan cut down a lot of time as she could just hand the care plan to any HP if needed.

Prior to the CC, HP participants such as the ILD Consultant recognised that there had been poor communication and a lack of joined up thinking. HP were in agreement with patient and carer participants about inefficiencies prior to the CC and that the CC had improved communication across the primary and specialist care setting:

"actually quite nice we don't generally get tho:::se we generally get you know the referral and then we have to ring up and get more information and find out you know do they know their (1) their prognosis and you know has has his advanced care planning been discussed etc etc so having to like tease all the information out and then sometimes when we get there actually bring up it they say that it hasn't been discussed even though sometimes the hospital say it has so it [the CC] was very helpful in that respect" (Community Palliative Care CNS)

All HP were in agreement that having the patient and carer at the CC, involved in planning and fully aware of treatment plans for the future, was very helpful and allowed concerns to be prioritised focussing on the patients' and carers' needs. The ILD Consultant felt that as the specialist centre, they did not have time to address palliative care needs in busy clinics. As a result, these needs had dropped to the wayside. He was grateful for H2H. He stated:

"certainly kno:::wing that that aspect of the care was being taken care of it's not (1) its just so difficult to provide that sort of level of fine deta:::il in this hospital with so many patients coming through and as a referral centre that there just isn't the the ma:::npower to be able to focus on that sort of (1) erm specific symptom control and again knowing that you guys are doing it is a is a is sort of (1) often then it removes that from something we need to worry about....." (ILD Consultant)

The many different ways of referring to community palliative care teams and the variance in the community support received was seen as a barrier to referral by the ILD teams. Patients receiving H2H had the H2H CNS making all the referrals to the appropriate community HP. She would also try

to ensure that the care remained co-ordinated by checking in with the patient at 2 weeks, one month and 2 months after the CC. Patients, carers and HP could contact the H2H CNS if there was a breakdown in care which she would try to resolve. This was reflected on by the GP who felt that co-ordination of care for patients who weren't involved in the study was "patchy" and "haphazard". The GP expressed that it was an unknown for patients, carers and HP as to which HP may be involved in the patient's care and a lottery as to which HP would subsequently visit the patient at home. He stated:

"if it wasn't for this (2) I can see a completely different scenario where this guy would be lost in the communityhe::: would be trying to find out who::: the respiratory nurse is [laughs] trying to get out who's the oxygen supplier trying to find out from his GP which one's going to be in charge of his care in the general practice which one's going to be helping him with his symptoms (1) you know it it would have become a hug:::e hassle and I don't think he::: realises how lucky he is actually to be part of this trial (2) because everything's there for him (2) there's no other issue..." (GP)

This was reiterated by the ILD CNS who felt that having the H2H CNS co-ordinate care and be available if needed gave extra support to patients and added an extra layer of support for the patient and carer to turn to if there was a breakdown of care in the community.

During the CC, HP were codified responsibility to address issues raised at the CC. In doing so, contact numbers were available to both the patients and carers for each HP and their allocated task. HP participants commented that having contact numbers of HP involved in patients' care clearly documented on the care plan was helpful. HP participants such as the community matron reflected on how she wasn't aware how to get in contact with the specialist teams prior to the CC and as a result would not have done. She felt that the contact numbers on the care plan facilitated approaching the specialist centre if needed and as a result improved care. Community HP interviewed also felt that having the H2H CNS at the CC fostered the relationship between the specialist and community settings and made it more likely that they would approach the specialist centre if needed for advice on how to manage the patient's care.

Interestingly, being involved in the study led to recognition by HP of the serious nature of the disease. As a result, not only did patients receive more HP input but patient participants and patients looked after by carer participants stated that they also gained easier/priority access. Carers such as Sue, 48 year old daughter of Mary who had NSIP, expressed that prior to the CC, she would often try to contact her GP at the local surgery which was often a time consuming and long process. However, post CC, things had improved immensely:

"the practice nurse has a system where something will come up where erm it's noted it will flag up that mum's in this home to care [H2H] process.....she can bypass a lot of the (1) the red tape" (Sue, 48 year old daughter of Mary with NSIP)

This was also recognised by the HPs interviewed. The GP commented that as a result of the study, patients had received FT access to all HPs. The GP reflected that this was empowering for the patient and carer. He stated:

"the patient is in charge of their own care:::for somebody like this yea:::h I think it's really useful for them because then (1) they can sort of direct their questions to the right people cause they're they're fully aware" (GP)

Theme 4 Crisis management

Carers such as Penny (63y wife of patient with IPF) felt that prior to the CC, they would have rung 999 if her husband needed help out of hours. All patient and carers expressed relief that the CC had set out clear crisis management plans with direct contact numbers for HP 24 hours a day:

"that's right (1) um (3) one of the things that I do (2) imme:::diately was that (2) as soon as I had the telephone number of one of the (1) people I contact, was straight into the into the telephone d- line, dial in directly (2) ah (2) both my old telephone [laughs] and my (1) mobile, so its its there so I can contact them."
(Alfred, 64 year old patient with advanced NSIP and no carer)

As did Peter, 63 year old with advanced IPF, who felt that having access to contact numbers and a clear crisis management plan was a vast improvement:

"and now I've got all erm (2) they as I say they phone and I've got er a whole list of numbers that I can phone any time day or night erm if I need to, you know"
(Peter, 63 year old with advanced IPF).

"do you find that helpful?" (SB)

"definitely] erm (1) it gives you (1) definitely gives you peace of mind, definitely"
(Peter, 63 year old with advanced IPF).

"... Do you think that er you would know what to do in a crisis no::w, so if something went wron::g?" (SB)

"oh yes yeah and (1) and (2) as I say I've got erm the telephone numbers... of of people that I can phone erm 24 seven which is ideal I mean before that erm the most I could do was dial 999" (Peter, 63 year old with advanced IPF).

In addition, HP such as the GP and ILD Consultant felt that having access to all the contact numbers was likely to help prevent hospital admissions.

Theme 5 Palliative Care and psychological support

Patients and carers felt that they had not been able to access palliative care prior to the CC. The main barriers to referral were misconceptions of what palliative care is and a misunderstanding of which patients were suitable for referral:

"our doctor we did speak to him (1) about (1) local care but our doctor actually said to us that they don't look at palliative care till you're bed ridden [laughs] (4) erm (4) but you need the support a long time before that (2) erm" (Leslie, 54 year old wife of Ted who had advanced IPF)

HPs were not the only ones that had preconceptions of palliative care. Patients and carers expressed that prior to the study they thought that a hospice would be somewhere where the "walking dead"

attended. Despite being involved in a palliative care study, some patients and carers were surprised to be contacted by the local hospice:

"we were a bit surprised er er to hear from the hospice (1) you know I mean er first first reactions when somebody (1) erm (1) one second [clears throat] wants to get a hospice involved you think like you've got to go in and er [laughs] you're not coming out" (Peter, 63 year old with advanced IPF).

Because of these misconceptions, patients and family members required repeated clear explanations of the remit of palliative care during the study. The appropriateness of palliative care/hospice teams in supporting patients for symptom control and psychological support throughout the disease journey was explained on entry to all patients and carers but needed to be repeated, especially if other family members became involved/attended the CC.

Interestingly, both patient and carer participants who had been hesitant of palliative care/hospice involvement at the start of the trial, subsequently expressed how much they valued the support they received from attending the day hospice and receiving regular palliative care input.

"I must say to everybody (2) definitely it is it's (2) I don't know how long I've got left but (2) whatever time I've got left (3) this palliative care is going to make that time better for me and it's better and if it's better for me it's better (2) for us as a family....I've been telling everybody (2) how important (3) you know I just wish I could get GPs in to buy into the (2) palliative care cause its makes such a difference (2) made such a difference to me" (Ted, 55 year old patient with advanced IPF)

In fact, being involved with the study and receiving community palliative care was seen as beneficial for both patient and carers in improving psychological symptoms. Sue commented that prior to the CC, her mother had been depressed. She felt that focussing on current and future care needs through the CC and accessing a support network had focussed her mother and improved her mood. Ted expressed that attending the day hospice allowed him to talk about his feelings if he wanted to:

"I have weeks when (2) er like last week I wanted to talk about (3) you know (2) my illness and stuff...and they're there then (2) for me to be able to tap into.. which I am happy for because (3) when you're in in my my sort of position when you know your life limited (1) is your life is limited often at home (3) you tend you live a lie say to people you live a lie I think because say how do you feel you just say I feel fine but because you don't want to be worrying people all the time but (1) when you've got a palliative care team round you you can get that out of your system which is something we didn't have for the first 18 months two years of this disease" (Ted, 55 year old patient with advanced IPF)

"do you mean that then you can be honest about how you feel?" (SB)

"yeah I can I they cause sometimes it's just about releasing it.... it's not it's not necessarily who you even talk to [laughs] it's yeah it's just somebody who cares but that means then I can come home and life is better at home" (Ted, 55 year old patient with advanced IPF)

Importantly, there was recognition that the disease affected the whole family and that support for loved ones and carers was needed. Support from the palliative care teams for carers was appreciated by both patients and carers:

"I started to go the day hospice once a week for 6 weeks and also er which I thought was a very good thing erm (1) they asked my wife if she wanted to go over there erm once a week erm (1) to a carers (1) erm (1) sort of meeting and er (1) also (1) erm (2) they they what else are they doing for her oh they do a she (1) tends to get swollen a ankles quite a bit erm and they (1) they massage them" (Peter, 63 year old with advanced IPF).

Theme 6 Symptom control

During the CC, the evidence based guidelines on managing the palliative symptoms of patients with ILD were distributed to all HP involved in the patient's care (whether attending the CC or not) and also

to the patient and carer. HP, patients and carer participants found these guidelines helpful. HP participants such as the GP felt the evidence based guidelines were useful in improving symptom control with clear options of what to prescribe patients if they deteriorate. The community palliative care CNS also felt that the intervention improved symptom control through increased confidence in their current practices and allowing community HP ready access to specialist teams in the hospital if needed. She stated:

"I think it was helpful to get because obviously we don't get a huge volume of these types of patients and er and therefore our knowledge isn't as great as as some of other knowledge on other patients that we get a lot of it was quite nice to know...we were given the exact plan for them really....it's quite nice to speak to a specialist and say you know what what particular drugs do you think work better you know we know what you use for ours but is there anything in particular and there wasn't anything hugely different but it's just nice to have somebody who specialises a bit more in the you know because the the diseases" (Community Palliative Care CNS).

ILD HP participants such as the ILD Consultant also felt that the intervention had been helpful in improving symptom control. He stated:

"we would start...with er symptom control in hospital whether that was a little bit of Oramor...ph or lorazepam and then it was really we wouldn't often see the patient for another 3 or 4 months time and it was then back to the GPs hands...to sort of titrate and change that as needed um and it didn't always go successfully the things weren't re-prescribed or wrong doses were given but knowing that er (1) you and your team are now doing that again we've had patients say that it's been very useful for them to have sort of continuity of care and someone taking overall view of that...." (ILD Consultant)

Carers such as Sue expressed that as a result of the CC she was made aware of all the options of delivery of care available to her mother. For example, she was not aware that if needed, her mother could have intravenous antibiotics at home so an admission to hospital was not always necessary. In

addition, having a documented clear strategy on how to manage each symptom within the care plan was seen as invaluable by all participants. Carers felt that it allowed them to manage their loved ones symptoms better and sometimes prevented hospital admission.

Theme 7 Empowering HP

The CC was seen as empowering by both the specialist and community HP participants interviewed. The ILD CNS commented on how a large part of her job as an ILD CNS was to deal with end of life issues and it was helpful to see how end of life conversations were handled by the H2H CNS. Being involved in the CC guided HP participants in how they ought to be conducting conversations around advance care planning:

"it's certainly enhanced my practice, um, certainly there's an huge (1) element of my job which is dealing with um the palliative care and end of life of patients, and I think, seeing how palliative care interact with patients and bring up (1) uncomfortable... (2) subjects for us as health care professionals, certainly has enhanced my practice....We need to... (1) understand that these aren't necessarily subjects that patients don't want to discuss...sometimes some of the anxiety around the issues can be discussing what the future is, discussing, (1) you know, having those uncomfortable conversations. I think, H2H has facilitated that, helped patients be more organised and think around what they're doing and also highlighted to us how to go about those conversations, and that those conversations are (1) ok to have." (ILD CNS)

All patients attending the Royal Brompton were given routine 3 monthly out-patient appointments in the ILD clinic. Previously, these patients had been reliant on attending these appointments, especially as there was little support being accessed in the community and patients did not have confidence in community HP in managing their disease. Through being involved in the study, patients and carers were linked in to their local community health services. Patient and carer participants reflected that they had started to develop support networks locally. This appeared to cause a change in the

relationship with the specialist centre where patients and carers began to question the aim of attending hospital appointments that were now viewed as stressful and burdensome:

"we are getting to the stage now (1) where (5) we won't be going to London so often I mean already xxxx has to go by (1) ambulance cause he's having 6 litres of oxygen... erm (3) and obviously as he gets more poorly you know the trips just really aren't going to be (3) er... (3) beneficial to to him.. but that's no because already now they're they're just really a chin wag across the table .. to and cause they can't do anything now.. so (2) to know that you've got what you need here now in xxxxxx you know right her... (2) is what we need you know not hundred miles down [laughs] the road" (Leslie, 54 year old wife of Ted who had advanced IPF).

This was also recognised by the ILD HP participants in the specialist centre:

"stratifying actually what (1) erm, (1) what hospital appointments patients are going to attend...has been very useful.....patients feel that they have to attend and then it's very stressful for them to make, you know make that trip in, so it's been very good for that angle as well." ILD CNS

However, even though patients and carers recognised that there wasn't anything that the specialist centre could do, they still preferred to have the option of being able to attend RBH (ie keeping it as a "safety net" if needed). Patient's and carers' confidence in the community teams was a gradual thing which seemed to develop over time as patients and carers had more contact with the HP. As confidence in the community teams grew, this affected whether they felt the need to attend out-patient appointments and investigations at the specialist centre. Appointments were often moved to 6 monthly and tests cancelled as patients and carers gained trust in the community HP and felt better supported. However, the "door was always left open" which was important for maintaining hope and patients' psychosocial wellbeing:

"patients when can't practically offer them any more treatment they're very reluctant to be discharged whether they've had a bad experience with their local

hospital or they (2) you know they think ok there might a new drug coming up round the corner" (ILD Consultant)

The initial CC with the H2H CNS was reassuring for GP and the other HPs. The community matron expressed that having a "specialist" (the H2H CNS) offer to give their mobile number and welcoming contact was very empowering to the community HP and instilled confidence in their abilities. The Community Palliative Care CNS reflected on how she hadn't always felt confident in dealing with these patients and how the CC helped in directing her in delivering appropriate care:

"we don't get a huge volume of these types of patients and er and therefore our knowledge isn't as great as some of other knowledge on other patients that we get a lot of it was quite nice to know erm the exact plan for them really..." (Community Palliative Care CNS)

The GP also commented that having easy access to specialists also made them more confident in delivering care as they knew that if there were any "issues, they had access to experts in the field".

Theme 8 Advance Care Planning

Previously, the two specialities of ILD and palliative care were not seen to run alongside each other and it was usually an either/or scenario. H2H appeared to help to assist in that transition and allowed palliative care to be introduced alongside attendance at the specialist centre whilst active ILD management was ongoing. In fact, patients were often still on active treatment such as pirfenidone when they were referred to the trial. The ILD Consultant recognised that the shift between discussing ILD treatment options and palliative care was one that was difficult to do therefore difficult conversations about palliative care were often avoided:

"because of the nature of this unit I don't think we deal that particularly well when we've run out of treatment options (2) to then put them onto a palliative care pathway and whether that's because they see different people and in different adm- you know different clinic visits (2) or if we ourselves as as health care professionals just don't like dealing with that kind of stuff...." (ILD Consultant)

ILD HP participants also recognised that important discussions surrounding advance care planning (such as preferred place of care and death) were not something that were done well by the ILD teams even though there was recognition that they were likely to prevent unnecessary hospital admissions. It was appreciated that the CC facilitated these discussions.

Through the CC, frank and open advance planning discussions were conducted. Prior to the CC, the H2H CNS (with a background in palliative care training) would ascertain with the patient whether they were happy to have discussions surrounding preferred place of care (PPC) and preferred place of death (PPD). Not all patients were ready to talk about PPC or PPD at the CC. However, patients and carers participants interviewed were grateful to talk about these issues- especially to find out more information about all the options available to them. Interestingly, the CC became a vehicle to facilitate frank and open discussion with family members which may not have occurred otherwise. The GP felt that the CC empowered patients to have conversations about end of life and to make sure that their views were communicated to their loved ones and the HP involved in their care.

Rachel whose mother had been going in and out of hospital for the last 2 years found the discussion and communication of the decision at the CC difficult:

*"mum has made up her mind that she doesn't want to go back to the hospital
erm mum wants to stay hom...e so erm I have decided as much as this is very
hard I've decided not to... fight against my mum's wishes (1) er...m (1) I do
understand that my mum's (2) condition (2) is (3) far gone" (Rachel, 47 year old
daughter of patient with advanced IPF)*

However, there was a realisation that even though the conversations were difficult, they needed to occur: Ted touchingly commented alongside Leslie on how the CC forced him to open up to his grown up children about the future:

*"...and that was the thing with the (2) I mean I did get upset at the initial (4) thing
sitting round the table but that was the first time and it was probably as much
because it was the first time (1) I'd had my children (3) the children were there
(3) but they're not children but my my children (2) there... erm I was able to say
anything (3) and tell them let them know how I really felt so that's why and you*

feel a bit weepy because you think (1) should be hiding it as a father you think (2) but it's not not (4) you know it's not you're not pre-programmed to (1) be talking about your own death...so (3) it's not an easy one to (1) discu::ss...so (2) that's the only (3) but I don't I think the (1) the way (1) you've brought everybody together is fine because you're also getting a shock to the system like I found but I'm just talking in front of [laughs] my children and kids so be completely open about it." (Ted, 55 year old patient with advanced IPF)

"and looking back (2) do you think that was a good thing?" (SB)

"oh definitely it was a good thing cause [it made]" (Ted, 55 year old patient with advanced IPF)

"I don't think] you would have (2) opened up [to them]" (Leslie, 54 year old wife of Ted who had advanced IPF).

"I don't think] I don't think I ever would have I don't think I ever would have opened up without (2) you setting (1) that (2) in place that's the thing (2) I don't I still think I would have been (2) yeah I'm feeling I'm not feeling very good or I'm feeling you know I'm feeling alright I still don't think I would have really faced up to it" (Ted, 55 year old patient with advanced IPF)

Leslie also reflected on her experience of advance care planning at the CC and the appropriateness of the timing of these conversations:

"for us it was a bit traumatic you know everything being coming to life that actually these things are happening I think you can go to hospital appointments and still sort of brush it aside that you know [laughs] erm (2) but once everybody was sat round the table and we talked about DNRs ...and erm (4) advanced directives and all this sort of stuff it did bring it home and it did get a little bit (3) upsetting but (3) I I still do believe that it was better at that point than when (1)

somebody's actual laid on their bed and you think it could be any da::y and (2) erm (1) you know I think you can deal with it better at that stage" (Leslie, 54 year old wife of Ted who had advanced IPF).

Interestingly, as patients developed closer relationships with community HP and especially the community palliative care team, this led to more discussions about end of life preferences and changed preferences. This may have reflected an increased confidence in the community teams and development of relationships with the community palliative care teams over time after the CC.

Theme 9 Feasibility and acceptability of the intervention

The timing of the intervention was thought to be appropriate and the earlier in the disease process it occurred, the more perceived benefit there was:

"it is (1) better (3) than (3) later you know if all these things happen once you're bed ridden (2) erm (3) you know you've got people coming in (2) that you don't know at least you know this way I mean we kno::w the nurses...you know we know them first name terms erm you know you you feel comfortable with them erm (5) you know I do thinks it's definitely it nee- it needs to be done that way erm and that much earlier." (Leslie, 54 year old wife of Ted who had advanced IPF).

The length of questionnaires was deemed to be acceptable. In addition, the interval between questionnaires was also deemed to be appropriate; a 4 week interval between questionnaires was felt to be adequate to capture any changes in symptom control or quality of life. In addition, the questionnaires used were also felt to assess change satisfactorily by patients, informal caregivers and HP with the right outcome measures being used. One patient (Alfred) had felt that there was some repetition between questions in outcome measures and had become confused at times as some measures had asked about experiences over last 3 days (POS) and others over last 2 weeks (SGRQ).

Patients and informal caregivers alike did not feel that the questionnaires caused distress. There was a recognition that questions about death and dying were necessary but patients and informal caregivers alike did not feel that these caused suffering.

At the CC, patients and informal caregivers as well as the HP were given the evidence based guidelines. Both patients and informal caregivers were grateful for the guidelines (even though they weren't specifically tailored to the lay person). Patients such as Alfred felt that they encouraged him to research areas that were not familiar but found it encouraging that he was using the right things in other areas.

All HP were extremely grateful for the guidelines. For example, the ILD Consultant found them very useful and he felt they allowed systematic evidence based symptom control rather than ad hoc delivery of symptom control as he had previously done. Generalists such as the GP found them invaluable and specifically appreciated having guidance from specialists which again reassured him and instilled confidence that he was doing the right thing and guided him on aspects of symptom control he wasn't sure about.

Patients and informal caregivers interviewed did not feel that there was any problem with the FT design. One informal caregiver in particular (Penny, wife of a 67 year old patient with IPF) did not feel it was a problem to have to wait one month for the intervention as she did not feel that her husband's prognosis was so short that waiting would matter. However, the Community Palliative Care CNS did feel that it mattered especially if a patient was particularly unwell, she felt the wait could affect the care:

"I do think with some of them that it would cause problems. Erm I think that it would have been too late particularly if they're very poorly.... and you can't necessarily predict that with everybody and actually some of them (1) 4 weeks (2) would be too much without all that help...." (Community Palliative Care CNS)

However, there was an understanding from those with a research background such as the ILD Consultant that 4 weeks was a reasonable time period for the WL group to wait before receiving the intervention as it often took longer than that to set up support in the community.

All patients and informal caregivers interviewed were grateful for having taken part in the study:

"...just to say I'd like to thank you erm (1) for giving me the opportunity to go on this in- like on this survey [study] and to get the help that I've I've now got I really do appreciate it....." (Peter, 63 year old with advanced IPF).

"I think the study's excellent" (Stephen, a 81 year old patient with NSIP)

In addition, HP also felt extremely positive about the CC and reported that patients and informal caregivers had fed back to them about their experience:

"we've had good (1) er quite a lot of good feedback from patients as well that it's been very useful for them with regards to symptom management and having someone coordinate their overall care" (ILD Consultant)

"on every level I found it very very (3) er::: (4) useful.....I think it's brilliant..." (GP)

I will now discuss the methods, results and discussion in greater detail:

5.4 Methods

5.4.1 Study Design

The study design used is a Phase II fast-track randomised controlled trial forming part of the **Feasibility and Piloting** stage of the MRC's guidance on development and evaluation of complex interventions. The main aim of a phase II trial is to identify therapies that warrant further investigation based upon acceptable side effects and promising efficacy. Additional purposes include assessing feasibility and acquiring further information about the intervention (such as acceptability).(158) A phase II trial highlights if an intervention may be potentially efficacious and warrants further study in a larger, appropriately powered phase III or **Evaluation** clinical trial.

When deciding on the trial design, the benefits and difficulties of experimental and quasi-experimental designs were considered.(159) It was decided that either a matched control group study or a randomised controlled trial (RCT) would be most appropriate. A RCT was chosen as it would decrease the effects of patient selection bias and increase ability to ensure that uniform evaluation criteria were used. It was felt that if the trial ran without randomisation, it would be difficult to conduct a RCT subsequently as staff may feel that there was a reduction in the service delivered which would then make recruitment to a phase III or **Evaluation** trial challenging. Also, subsequently it would be problematic to find a suitable non-random comparison group. In the Fast-track RCT design all patients have the possibility to receive the intervention, some immediately, and other after a wait (equivalent to a normal wait within the NHS for PIF-ILD patients). A Fast-track trial has previously been used successfully by Higginson et al in delivering a palliative care service to Multiple Sclerosis patients.(159) A Fast-track RCT was agreed as it provided the rigour of a RCT whilst allowing all patients to receive the intervention. It was felt that if all the patients were to receive the intervention, this would maximise recruitment and referral from ILD HPs. The pros and cons of both a matched controlled and Fast-track design RCT that were considered are depicted in Figure 5-2 Page 221.

Figure 5-2 Pros and cons of using a matched control design compared to a FT randomised controlled trial design as applied to the PIF-ILD H2H intervention

Matched Control Group	FT Randomised Control Trial
Patients at other hospitals are unlikely to be comparable to RBH patients	<i>Using patients from RBH throughout study</i>
Not everyone will receive the service	<i>Everyone will eventually receive service</i>
<i>No issues with patients dying before receiving intervention</i>	Patients may die before intervention received
Realistic F/U time period needed	Intervention must show result before crossover period
HP in the control group may change their practice	Members of CC might be involved in looking after patients in both the WL group and FT group which may bias results
<i>Has been used in H2H cancer study</i>	<i>Used successfully previously in palliative care in Multiple Sclerosis(159) and Breathlessness Intervention Service studies</i>

Pros are shown in italic, Cons in bold

Mixed methods were used in his study combining a quantitative trial with in-depth qualitative interviews. I will now present the methods for the quantitative trial followed by the methods for the qualitative interviews. I will then discuss criteria for both feasibility and acceptability that were used and what information was collected to inform a future **Evaluation** trial.

5.4.2.1 Setting and Participants

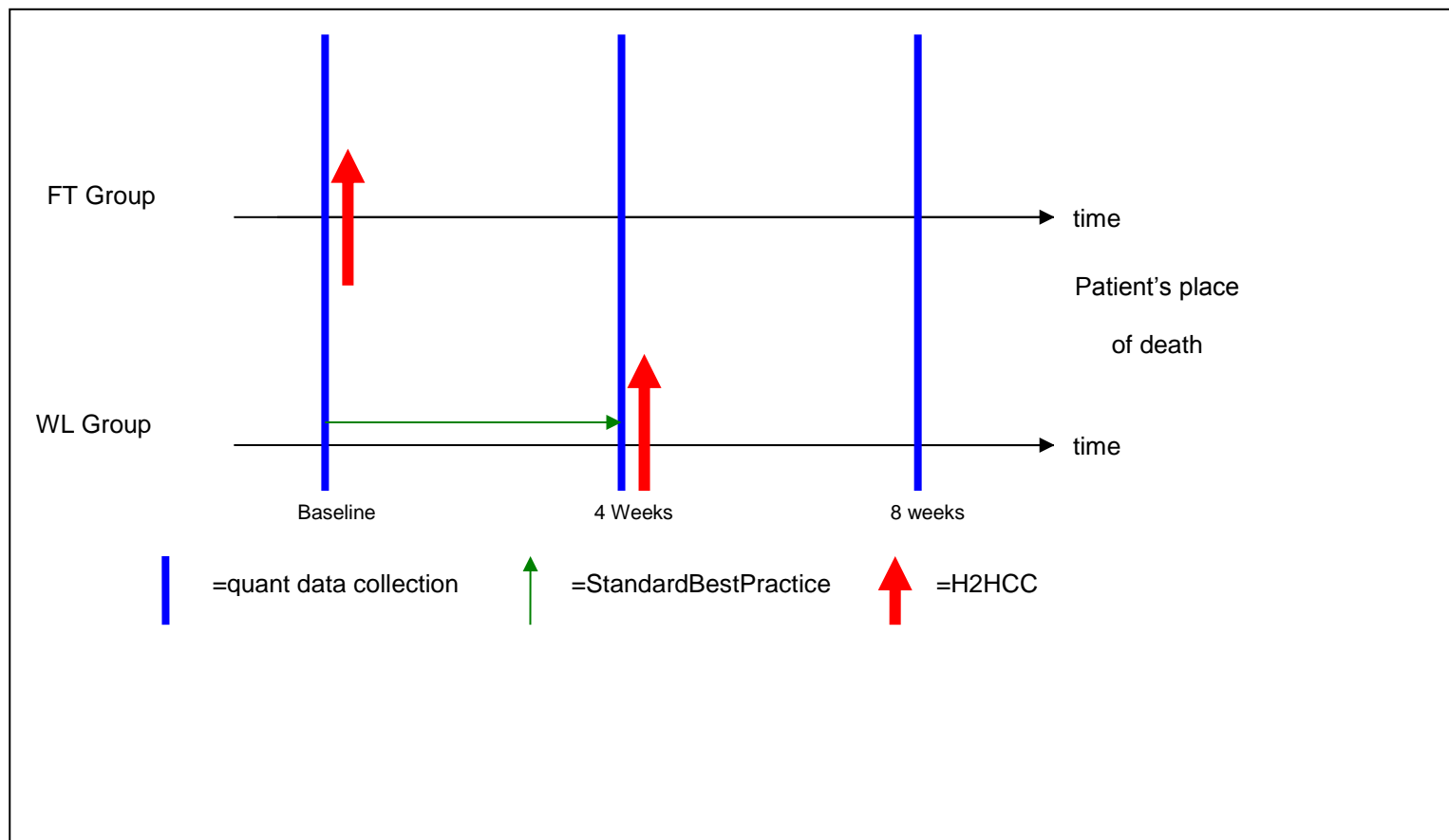
Patients were approached for recruitment if they had a clinical diagnosis of PIF-ILD (IPF (diagnosed using ATS/ERS criteria(160)) or fibrotic Non Specific Interstitial Pneumonia (NSIP)) and the following prognostic parameters: extensive disease (>60%) or honeycombing (>35%) on HRCT or CPI >50. Previous staging work done has shown that this group of patients have a 30% survival at one year and a 10% survival at two years. (APPENDIX C-5) Patients were identified by either the ILD or clinical palliative care teams at RBH from either the inpatient or outpatient setting. Patients were initially approached about the study by their clinical teams and if patients were interested in taking part, their details were passed on to me. At this point I would approach and screen patients for suitability. The informal caregivers of these patients were also approached. Where possible, dyads of patients and informal caregivers were recruited. However, if informal caregivers did not wish to take part or patients did not have an informal caregiver, this did not exclude patients from taking part. Patient and informal caregiver participants were excluded if they were less than 18 years old, they did not have capacity to consent or if they did not have adequate understanding of written English to complete the questionnaires.

5.4.2.2 Study protocol

The full protocol is available in APPENDIX C. A summary will be provided here:

After providing consent and baseline interview, patients were allocated to Fast Track (FT) or Waiting List (WL) by independent off-site computerised randomisation. If patients were randomised to FT, their information was passed to the H2H nurse to organise a CC as soon as possible. If patients were in the control arm, they continued to receive Standard Best Practice (SBP) for 4 weeks. After this time, they received the intervention and were interviewed and followed up as for the FT group (see Figure 5-3 Page 223 and APPENDIX C-1b)

Figure 5-3 FT RCT design and timing of intervention with outcome measurement



5.4.2.3 The intervention

Patients affected by PIF-ILD received a range of services (Standard Best Practice SBP). These were available to all those who received H2H immediately or after a delay. Services included general practitioners, physiotherapy and respiratory services and community palliative care teams. All had seen an ILD physician at RBH preceding referral and remained under specialist care with access to in-patient care as appropriate. H2H was offered in addition to the SBP services outlined. H2H aimed to complement the existing local services and not to duplicate or replace them. Preliminary qualitative **Development** work conducted identified that evidence based guidelines for the management of the physical, psychological, spiritual and end of life-planning needs for these patients was needed. These guidelines were developed and used as part of the H2H CC. (APPENDIX B). The guidelines permitted a structured and evidence based practice in delivering palliative care to these patients where there had previously been none. The written guidelines acted as a supplement to the actual assessment. With the patients consent, a CC was organised in their home (or place of their choice). The patient, informal caregiver, H2H Clinical Nurse Specialist (CNS), GP, district nurse, respiratory nurse, community palliative care nurse and any other health or social care professional closely involved in the patients care were invited to attend. If patients weren't already under the care of these community HPs, referrals were made by the H2H CNS.

At the CC, current and anticipated care needs were discussed, and an action plan agreed allocating a responsible HP for each item. During the CC, individualised care plans were made. The care plan aimed to provide a quality comprehensive Palliative Care assessment with clear action plan. This was then communicated with local services, both primary and specialist teams aiming to result in streamlining of transfer of data and codifying responsibility for the patient, hospital and community care professionals. The aim of the CC was to enable improved symptom control, QoL, crisis prevention and decreased hospital admissions. In addition, this intervention aimed to manage uncertainty by facilitating early discussion about disease progression, improving communication and addressing end of life planning needs. The H2H CNS followed up each CC (at 2 weeks, 1 month and 2 months) with the patient or informal caregiver. The ongoing palliative care of these patients were delivered by the community palliative care team as deemed appropriate by them.

The intervention was delivered by a H2H CNS using a standardised proforma for the CC and for follow up contacts (APPENDIX C-2a, 2b, 2c). In addition, the H2H CNS used the evidence based guidelines (APPENDIX B) to help ensure uniformity of advice given during the CC to patients, informal caregivers and HPs. The H2H CNS received training in the delivery of the CC from a number of H2H CNSs who were already using the intervention in the cancer setting at the Royal Marsden Hospital. This included multiple observations and observed delivery of the CC with constructive feedback.

5.4.2.4 Quantitative data collection

As recommended by the MOREcare guidance (14), where possible, outcome measures that have established validity and reliability in the PIF-ILD population, that are responsive to change over time, capture clinically important data, are easy to administer and interpret, are applicable across care settings and are able to be integrated into clinical care were selected.

5.4.2.4.1 Primary outcome

The primary outcome was to compare the change in Palliative Care Outcome Scale scores from baseline for each group at 4 weeks (4 weeks after the intervention for FT group and just before the intervention for the standard best practice group). The POS was developed in advanced cancer patients and includes aspects about pain and symptom control, patient and family psychosocial needs, and communication and information needs.(161) An adapted version which took account of the most common symptoms in this disease group was used in this study to provide an assessment of change in palliative care needs (including symptom control) (APPENDIX C-11). The adapted POS used contains eight questions on anxiety, patient and informal caregiver concerns, and practical needs, each rated 0-4. It could be completed by the patient or informal caregiver. The scoring system ensured that there was some ongoing data available if the patient became unwell and was no longer able to complete the study. The POS was thought to be an appropriate primary outcome as it assesses overall palliative care need. The **Development** work had shown that patients and informal caregivers affected by PIF-ILD are affected holistically and the focus of their need is not just symptom control. There are no holistic palliative care measures validated in ILD.

5.4.2.4.2 Secondary outcomes

Outcome measures used in the cancer H2H model were preferred to allow comparison of the H2H intervention between the cancer and PIF-ILD population. However to allow comparison to other interventions previously used in PIF-ILD, some outcome measures were replaced as informed by the systematic review conducted in Chapter 1. The systematic review showed that within each symptom, there was a wide range of outcome measures used with no uniformity or consensus on the most appropriate measures. Dyspnoea and QoL were the most reported outcome with eleven and six different outcome scales used respectively. Table 5-1 Page 227 shows the table from the systematic review showing the different outcome measures used in interventions to improve symptoms and QoL in PIF-ILD.

Table 5-1 Table to show different outcome measures used in interventions to improve symptoms and QoL in PIF-ILD

Type of outcome measure	Symptom	Outcome measure	Papers using outcome measure
Symptom control	Dyspnoea	Borg Dyspnoea Index	Krowka 2007(162), Ozalevli 2010(163), Zisman 2010(164), Hicks 2007(165), Collard 2007(166), King Jr 2008(167), Raghu 2010(168), Rammaert 2009(169), Jackson 2010 (170), Visca 2011(171)
		Medical Research Council Scale	Antoniou 2006(172), Holland 2008(173), Ozalevli 2010(163), Varney 2008(174), Rammaert 2009(169), Kozu 2011(175), Strieter 2004(176)
		Baseline Dyspnoea Index	Nishiyama 2008(177), King 2011(178), King Jr 2008(167), Raghu 2010(168), Strieter 2004(176), Rammaert 2009(169), Kozu 2011(175)
		Transition Dyspnoea Index	King 2011(178), King Jr 2008(167), Raghu 2010(168), Strieter 2004(176), Kozu 2011(175)
		Visual Analogue Scale	Rammaert 2009(169), Allen 2005(179)
		4 step improvement in dyspnoea scale	Turner-Warwick 1980(180)
		5 point dyspnoea scale	Agusti 1993(181)
		20 point dyspnoea scale	FioruCCi 2008 (182), Demedts 2005 (183), Undurraga 1998(184)
		University of California San Diego Scale	Zisman 2010(164), King 2009(185), Lindell 2010(113), Strieter 2004(176), Noble 2011(186)
		NYHA	Krowka 2007(162) Hanania 1993(187)
		Mahler Dyspnoea Scale	Raghu 2008(188)
	Cough	Visual Analogue Scale	Hope-Gill 2003(189)
		Leicester Cough Questionnaire	Lutherer 2010(190)
		Question 2 on St George's Respiratory Questionnaire	Horton 2008 (191)
	Depression	Dry, productive or absent	Antoniou 2006(172)
		HADS	Rammaert 2009(169)
		Beck Depression	Lindell 2010(113)
		Patient Health Questionnaire-8	Swigris 2011(192)
	Anxiety	Beck Anxiety	Lindell 2010(113)
		General Anxiety Disorder-7	Swigris 2011(192)
	Fatigue	Fatigue severity scale	Swigris 2011(192)
	Sleep	Pittsburgh Sleep Quality Index	Swigris 2011(192)
QoL		SF36	Holland 2008(173), King 2011(178), Zisman 2010(164), King Jr 2008(167), Raghu 2010(168), Raghu 2008(188), Rammaert 2009(169), Swigris 2011(192)
		SF-36 Japanese version	Kozu 2011(175), Tomioka 2005(193)
		SF-36 Turkish version	Ozalevli 2010(163)
		St George's Respiratory Questionnaire	Nishiyama 2008(177), Antoniou 2006(172), Varney 2008(174), Zisman 2010(164), King 2009(185), King Jr 2008(167), Raghu 2010(168), Demedts 2005(183), Raghu 2008(188)Rammaert 2009(169), Mishra 2011(194)
		EQ5D	King 2011(178), Zisman 2010(164)
		Chronic Respiratory Disease Questionnaire	Holland 2008(173)

The choice of outcome measures for the feasibility/pilot RCT and rationale is explained in Table 5-2 Page 228. This is followed by detailed discussion of each measure to be used.

Table 5-2 Outcome measures for Feasibility and Piloting stage and rationale for use

BASELINE CHARACTERISTIC/OUTCOME	INSTRUMENT/MEASURE	RATIONALE FOR USE OF MEASURE
PATIENT		
Patient Palliative Care Needs	Palliative Care Outcome Scale(161) with symptom question including most common PIF-ILD symptoms- breathlessness, cough, fatigue, insomnia (to be completed by patient and carer)	Includes aspects about physical needs, patient and family psychosocial needs, and communication and information needs. Validated in cancer.
Patient breathlessness at best/worst	Visual Analogue Scale(195) and D12 scale(196)	VAS used in previous PIF-ILD studies D12 used in H2H cancer trial
Patient Qol	KBILD(197) and St Georges Respiratory Questionnaire SGRQ(198)	KBILD validated in PIF-ILD population SGRQ used in previous PIF-ILD studies
Patient functional ability	Palliative Performance Scale(199) MRC breathlessness scale(200)	PPS used in H2H cancer trial MRC breathlessness scale used in previous PIF-ILD studies
Patient anxiety	Hospital Anxiety and Depression Scale (201)	Used in previous PIF-ILD studies and H2H cancer study
Patient use of other services	Service use questions	Used in H2H cancer study
Preferred place of care and death		Used in H2H cancer study
CARER		
Carer Qol	Caregiver Qol Index (202)	Used in H2H cancer study
Carer anxiety	Hospital Anxiety and Depression scale (201)	Used in H2H cancer study
Carer's assessment of patient's use of services	Service use questions	Used in H2H cancer study
Carer burden	Zarit Burden Inventory(203)	Used in H2H cancer study

VAS: Visual Analogue Scale for breathlessness.(195) The VAS is a vertical line 150mm long with anchors at each end to indicate the different levels of breathlessness. The VAS used in this study had levels of breathlessness of none, slight, moderate, severe and extreme. The subject was asked to mark a point that indicated the amount of breathlessness experienced at the time.(204) As breathlessness is a sensation that can change between measurements, the VAS is most suited to within-subject repeated measurement as it has the sensitivity required to measure minute changes.(205)

D12 Scale: D12 scale is an overall score for breathlessness severity that incorporates seven physical items and five affective items.(196) Participants complete the D-12 in reference to their experience of breathlessness “these days” at baseline and follow-up. D-12 consists of 12

descriptor items on a scale of none (0), mild (1), moderate (2), or severe (3). The time reference period for “these days” captures the current level of breathlessness experienced by patients as opposed to specifically on the day of the test or in response to a specific activity. Total scores from the D-12 range from 0 to 36, with higher scores corresponding to greater severity.

K-BILD: The King’s Brief Interstitial lung disease (K-BILD) is a 15 item questionnaire consisting of three domains (breathlessness and activities, chest symptoms and psychological).(197) It has been validated in all ILD disease groups including IPF. A higher score indicates a higher QoL. Scores range from 0-100 with the minimal important difference (MID) having been calculated as 8 units of the total score.(206)

SGRQ: St George’s Respiratory questionnaire (198) is a 50 item instrument designed to measure impact on overall health, daily life, and perceived wellbeing in patients with obstructive airways disease. Part 1 has a symptoms component (frequency and severity) with a 1, 3 or 12 month recall (several scales); Part 2 has a activities component looking at activities that cause or are limited by breathlessness and an impact component looking at social functioning, psychological disturbances resulting from airways disease and referring to current state as the recall (dichotomous (true/false) except last question (4 point Likert scale).(207) The MID for IPF in each of the SGRQ domains is Symptoms 8 units, Activity 5 units, Impact 7 units and Total 7 units.(198) A lower score indicates a better QoL. The generic SGRQ has been validated in IPF.(198)

PPS: The purpose of the Palliative Performance Scale (PPS) is to assess the physical condition and functional status of persons receiving palliative care. Scores may range from 0 (dead) to 100 (normal functioning).(199) The PPS measures three broad areas of function: intake, level of consciousness, and mobility. The PPS is scored from 0–100% at 10% increments. The PPS level for a given patient is determined by reading across the table at each 10% decrement to find the overall best fit. 'Stronger' performance factors are noted to be located on the left of the instrument 'softer' ones on the right. Patients who have a lower PPS generally are more

functionally impaired than those with higher scores. Prognosis is generally related to functional status in most palliative care patients. PPS has not been validated in ILD patients.

MRC Dyspnoea scale: Medical Research Council (MRC) dyspnoea scale (score range, 1-5, with higher scores indicating greater impairment) (200) is used to classify participants according to activity limitation. The MRC scale comprises five statements that describe almost the entire range of respiratory disability from none (Grade 1) to almost incapacity (Grade 5). It is self-administered by asking subjects to choose a phrase that best describes their condition. The MRC breathlessness scale does not quantify breathlessness itself. Rather, it quantifies the disability associated with breathlessness by identifying that breathlessness occurs when it should not (Grades 1 and 2) or by quantifying the associated exercise limitation (Grades 3–5). It has not been validated in ILD patients.

HADS: The 14-item Hospital Anxiety and Depression Scale (HADS) is a widely used tool for assessing psychological distress.(201) The HADS comprises seven items that tap anxiety (score range, 0-21) and seven items that tap depression (score range, 0-21), with higher scores corresponding to greater distress. The HADs may be completed by both patient and informal caregiver. The HADs has not been validated in IPF. The MID in COPD is 1.5.(208)

CQOLC: The Carer Quality of Life Cancer (CQOLC) measures four conceptual domains of QoL: physical functioning, emotional functioning, family functioning and social functioning.(202) The CQOLC consists of 35 items that have a five-point Likert format that range from 0 (not at all), 1 (a little bit), 2 (somewhat), 3 (quite a bit) and 4 (very much): ten items relate to burden, seven to disruptiveness, seven to positive adaptation, three to financial concerns and eight single items to additional factors (disruption of sleep, satisfaction with sexual functioning, day-to-day focus, mental strain, informed about illness, protection of patient, management of patient's pain and family interest in caregiving). The CQOLC scale is scored by adding up the score on each item to yield a total score for the instrument and scores can range from 0-140. For all items and domains that measure QoL, a higher score represents a better QoL.(202) There is no current

tool to measure informal caregiver QoI in non-malignant respiratory disease. Therefore the CQOLC was used which has been validated in cancer patients. Informal caregivers were clearly informed that the patient did not have cancer.

ZBI: The Zarit Burden Interview (ZBI) was developed to measure subjective burden among informal caregivers of adults with dementia.(203) Items were generated based on clinical experience with informal caregivers and prior studies resulting in a 22-item self-report inventory that examines burden associated with functional/behavioural impairments and the home care situation. The items are worded subjectively, focusing on the affective response of the informal caregiver.(209, 210) Each question is scored on a 5 point Likert scale ranging from - never to nearly always present. Total scores range from 0 (low burden) to 88 (high burden). There is no validated tool to measure caregiver burden in ILD.

Primary and secondary outcome data were collected at baseline, 4 weeks and 8 weeks as shown in Figure 5-4 Page 232.

Timeline	FT (immediate referral to H2H service)	Standard Best Practice (WL group)
Consent and Baseline Interview	(a)	
Randomisation		
Week 1	B	
Week 2		
Week 3	C	
Week 3		
Week 4	(d)	
Week 4		B
Week 5	E	
Week 6		C
Week 7		
Week 8		E
Week 8	(f)	
Week 9	G	
Week 12		G
Death	Place of death documented	

(a)	Baseline research interview and consent on entry to the study before randomisation
B	H2H CC arranged and conducted
C	2 week post CC F/U by H2H CNS
(d)	Week 4 repeat of baseline interviews (for WL group, this would be pre H2H CC)
E	1month post CC F/U by H2H CNS
(f)	Week 8 repeat of baseline interviews
G	2 months post CC F/U by H2H CNS

Figure 5-4 Graphical depiction of H2H intervention and outcome measurement in FT versus WL group

5.4.3 Qualitative component of RCT

5.4.3.1 Settings

Patients and informal caregivers were recruited from those who had completed the trial. Participants who the H2H CNS felt would be amenable to taking part in qualitative study were approached. All interviews except for 3 (HP2, HP3 and HP4) were conducted by myself. A Specialist Registrar from the Royal Marsden Hospital (Neil Nijhawan) who had attended a qualitative interview course and been trained (including practice and observation interviews) by myself in qualitative interviewing conducted the other 3 interviews.

All interviews were conducted in the patients' and informal caregivers' homes and HPs' work places. The patients and informal caregivers were already aware of my role within the research team. Where possible, participants were interviewed on their own to ensure that there was minimal bias. This was possible for all interviews. Informed consent was obtained prior to starting the interview. Whilst obtaining informed consent and prior to starting the interview, participants were assured that they could request for the interview to be stopped at any stage and for any reason.

5.4.3.2 Topic guide

The interview broadly followed the topic guide shown in Figure 5-5 Page 233 and APPENDIX C-4. This was developed based on the literature and discussion with experts on the Project Advisory Group. The interviews were semi-structured so even though the topic guide provided direction and highlighted areas that needed to be addressed, I was able to be led by the participants on discussing areas they felt to be important and relevant.

Figure 5-5 Topic guide for in-depth interviews for RCT

- | |
|---|
| <ul style="list-style-type: none">• What do you feel are the most important aspects of Hospital2Home (H2H)?
Prompts: evidence based guidelines, codifying responsibility, multi-professional working, crisis management, advance care planning• What have you found particularly helpful?
Prompts: evidence based guidelines, codifying responsibility, multi-professional working, crisis management, advance care planning• Is there anything about the intervention that you found unhelpful?• What if any improvements would you like to see in the H2H model of care? |
|---|

5.4.3.3 **Conduct**

The interview process began by introducing the research and who I was. It was made clear that all data would be anonymised and kept completely confidential from anyone outside the research team. It was explained that the interview would be audio recorded and that if there were any questions that the participant did not wish to answer, then they could choose to omit or terminate the interview. In addition, it was explained that if the participant required a break or had any questions which they did not wish to be part of the interview, then the interview could be stopped.

Recordings were made using a small unobtrusive digital recorder which was placed between myself and the participant. No one objected to the interview being recorded nor did anyone ask for the recording to be stopped during the interview.

Participants appeared motivated to help take part in the interviews largely because they wanted to feed back about the intervention.

5.4.4 Feasibility

There is no detailed description in the MRC guidance on how feasibility of a complex intervention should be measured and appropriate reference points at which an intervention is deemed feasible. It was also noted by Bugge et al (211) that there is no systematic guidance on how to categorise and explore issues that have arisen related to feasibility. However, Shanyinde et al (212) reported 14 issues that need to be evaluated in feasibility or pilot studies. These are shown in

Figure 5-6 Page 235 and will be used to analyse and present the feasibility data.

Methodological issues
1. Did the feasibility/pilot study allow a sample size calculation for the main trial?
2. What factors influenced eligibility and what proportion of those approached were eligible?
3. Was recruitment successful?
4. Did eligible participants consent?
5. Were participants successfully randomised and did randomisation yield equality in groups?
6. Were blinding procedures adequate?
7. Did participants adhere to the intervention?
8. Was the intervention acceptable to the participants?
9. Was it possible to calculate intervention costs and duration?
10. Were outcome assessments completed?
11. Were outcomes measured those that were the most appropriate outcomes?
12. Was retention to the study good?
13. Were the logistics of running a multicentre trial assessed?
14. Did all components of the protocol work together?

Figure 5-6 Methodological issues for feasibility of research highlighted by Shanyinde et al.

In addition, time taken to arrange H2H CC, length of interview, deviations from H2H CC protocol and uncompleted CCs and reasons why amongst other details were recorded. A full list of details recorded are shown in Figure 5-7 Page 236.

Pre CC	Registered with appropriate GP?		
	Involvement of HP prior to randomisation- district nurse, community matron, community respiratory nurse, community palliative care?		
	Referrals and designation of HP referred to by H2H CNS		
	Refusal of any HP to accept referral	Designation	Reason why
	Total time taken to set up CC		
CC	Time taken from randomisation to CC		
	Reason for delay if any		
	Length of CC		
	Number of relatives and designation of HP present		
	Symptom control discussed?	Number of symptoms	Which symptoms
	Positive feedback about CC?	Who from	Comments made
	Negative feedback about CC?	Who from	Comments made
	H2H CNS comments re CC		
	PPC (Preferred Place of Care) discussed at CC?	If No, why not?	PPC at time of CC
	PPD (Preferred Place of Death) discussed at CC?	If No, why not?	PPC at time of CC
Post CC	Did patient have an unplanned admission post CC and before trial completion?	If so, for how long?	Was reason anticipated in care plan?
	H2H CNS contacts outside of regular follow up (total in mins)		
	Did patient have booked OP/IP/investigations which were cancelled post CC?	If yes, reasons for cancellation	
	Date of death		
	Number of days from CC to death		
	Number of days in PPC		
Death	PPC achieved?	If not, why not?	
	PPD achieved?	If not, why not?	
	Did PPD change after CC?	Details	
	Place of death		

Figure 5-7 Information recorded about Case Conference (CC)

There were no reference points in the literature on when a trial involving a complex intervention ought to be deemed feasible. Decisions about feasibility appear to be individual. For this trial, the trial will have been deemed to have been feasible if all three of the below criteria are met:

- Consent rate of patients is at least 25%
- There is recruitment of 52 patients over time period of the trial
- 80% of patients in the FT group were able to receive the H2H intervention within 14 days of their allotted time.

5.4.5 **Acceptability**

There is no formal guidance within the MRC guidance on how acceptability ought to be measured. However, previous trials (213, 214) looking at acceptability of complex interventions using MRC guidance have looked at using a mixed methods approach with incorporation of both quantitative data (such as attrition rates) and qualitative interviews. Interestingly, I could find no reference point in the literature about levels at which an intervention would be deemed to be acceptable.

For this trial, in addition to collecting recruitment and retention rates, a qualitative approach was used in the post-trial evaluation to assess the acceptability of the intervention for patients, informal caregivers and HPs using the topic guide shown in Figure 5-5 Page 233. In addition the H2H CNS recorded her experiences of delivering the intervention and observations of patients' and informal caregivers' responses during and after the CC was delivered.

5.4.6 **Informing a future larger evaluation trial**

The following information was recorded to inform a future larger evaluation trial:

- exclusions, and drop-out rates
- interpretation of study information
- views of study design and outcome measures
- problems with completing measures, including missing data.

5.4.7 **Sample size and recruitment**

Phase II studies are exploratory. They are not powered to provide a definitive answer of efficacy compared to standard treatment. However, they may be used to be to conduct exploratory analyses which may help to inform a future exploratory trial.(158) There is no robust data to enable calculation of precise sample size needed to identify a significant change in POS scores between each arm. As such interpretation of the analysis was treated with caution but it was thought that it may be helpful in hypothesis generating and in providing estimates of effect size for a larger evaluation RCT. As stated in the MOREcare guidance (14), it is important to estimate in advance levels of attrition and integrate these into sample size estimates. I

anticipated recruiting 26 patients per group ie 52 in all. Based on the local patient numbers, I estimated to identify 2 patients per week, and recruit and retain at least 1 each week giving 52 patients in one year. I anticipated that this number was sufficient to estimate the change in POS score between baseline and 4 weeks with reasonable precision (assuming a standard deviation of 2, a 95% confidence interval for the difference between the intervention and usual care group would be 2.2 units wide ie mean difference \pm 1.1 units, which I judged to be sufficiently precise). It was recognised that the POS data were likely to be skew and the study would allow time to identify the most appropriate way to analyse these data for a later larger evaluation study.

Anticipated recruitment for the qualitative work was 15 (5 patients, 5 informal caregivers and 5 HPs).

5.4.8 Randomisation

Randomisation was provided by The Institute of Cancer Research - Clinical Trials and Statistics Unit (ICR-CTSU). Treatment allocation (FT/WL group) was by computer generated random permuted blocks with stratification dependent on severity of patient POS at baseline (patients with a POS score of equal or greater than 28 were classed as severe).

5.4.9 Amendments to protocol

After completing the systematic review (215) in Chapter 1, it came to light that the McGill Quality of Life questionnaire was not an appropriate QoL measure. The systematic review showed that this was not a measure that had been used previously in interventional studies in PIF-ILD. Therefore comparison of the H2H intervention in changes of score with previous interventions would not be possible. I therefore decided to use SGRQ instead as it would enable comparison with a number of other interventional studies. This amendment was made after recruitment and completion in the trial of the first patient.

During the course of the trial, it became apparent that it was extremely difficult to get the CC for those patients who are randomised to the FT group organised within one week and sometimes the WL group's CC at exactly 4 weeks. An amendment was therefore filed after recruitment of

the first patient to allow flexibility in the time points of the CCs and the assessments to be able to capture the data pre and post CC.

Patients with PIF-ILD who fulfilled the diagnostic criteria but did not necessarily rate as having extensive disease were being referred to the study. These patients had clear specialist palliative care needs. As recruitment had been slower than expected, an amendment was filed requesting to recruit these patients. All patients recruited continued to be scored on the prognostic scoring system (APPENDIX C-5). Amendments to protocol approval letters can be found in APPENDIX A.

5.4.10 Data Analysis

The primary endpoint for quantitative analysis was the change in total POS score (Baseline to 4 Week) which was compared between groups. Independent sample t-test were used to compare POS total scores between the FT and WL group at 4 weeks (before the WL group received the intervention). For all other outcome measures, mean scores with standard deviations at week 4 and week 8, mean change scores with standard deviations from baseline to week 4 and where appropriate, intervention effect size at week 4 are presented. If assumptions of normality were not met, non-parametric methods of analysis were used. Only patients with week 4 data were included in change analysis. The extent of missing data was explored and reflected on to assess whether occurred at random or whether there was a systematic pattern (whether data was missing at random or not, influenced how it was handled). The nature of missing data was classified and then a decision on how it was handled was made. Descriptive statistics were used to report time taken to organise H2H CC, time and duration of CC and time taken in follow up. All quantitative data were analysed using SPSS v 20.

All interviews were digitally recorded and then transferred verbatim onto a secure transcription database at the Royal Marsden NHS Foundation Trust. A palliative care secretary, who received appropriate training, transcribed the 15 interviews verbatim. All interviews were anonymised. During this process I listened to all tapes to identify the initial themes. I analysed transcripts line by line and coded relevant themes and categories into a coding framework developed *a priori* and built on during coding. The coding framework is shown in Figure 5-8

Page 240. Emergent themes were discussed with supervisor JK. Analysis of the data was conducted using a constant comparison approach (132) within Framework analysis as described by Ritchie and Spencer.(133) A number of stages were undertaken in this process and these were familiarisation, identifying a thematic framework, indexing, charting and finally mapping and interpretation (described fully in Chapter 4). All qualitative data were analysed using NVivo 9.

In keeping with the mixed methods approach, analyses is first presented as quantitative baseline clinical and demographic data and then drawing on both quantitative and qualitative data, I have compared and contrasted the quantitative findings with the findings from the qualitative work. The systematic comparison across data sources enabled me to begin to explain the nuances of outcomes and reasons why we may observe them and to begin to understand how the intervention may be working.

- 1. Overall positive comments about H2H**
- 2. Negative comments about H2H**
- 3. Possible effects of H2H CC model:**
 - i. symptom control
 - ii. psychosocial wellbeing
 - iii. communication between patient and family
 - iv. communication between HP
 - v. codifying responsibility
 - vi. linking in to community services
 - vii. change in relationship with specialist ILD service at RBH
 - viii. multi-professional working
 - ix. co-ordination of care
 - x. crisis management
 - xi. advance care planning
 - xii. efficiency
- 4. Ways in which H2H could be improved**
- 5. Feasibility/acceptability of CC**
- 6. Feasibility/acceptability of study design**
 - Fast-Track design
 - Appropriate outcome measures
 - Timing of questionnaires
- 7. Burden of questionnaires**
 - Length
 - Number of times needing to be completed
 - Distress caused

Figure 5-8 Coding framework for qualitative interviews in RCT

5.4.11 **Consent and ethical approval**

Prior to enrolment, written informed consent was obtained from all patients, informal caregivers and HPs. The study was approved by the NRES Ethics Committee London – Chelsea (ref number 11/LO/0999). Submitted and approved ethical approvals and amendments are in APPENDIX A.

5.5 Results

5.5.1 Quantitative results

Figure 2 in the published paper shows the CONSORT diagram of flow of patients through the study.

5.5.1.1 Baseline measures

Table showing baseline demographic and clinical characteristics for patients and informal caregivers are presented in the published paper as Table 2.

At baseline, patients were found to be similar in age, sex and ethnicity. In addition, there was a similar distribution of disease group and disease severity (as measured by TLCO, CPI and extent of disease on CT). However, the FT group appeared more likely than the WL group to have co-morbidities FT 17 (65%) vs WL 13 (48%).

5.5.1.2 Implementation of intervention

25 patients in the FT and 24 patients in the WL group received the CC. Table 5-3 Page 244 shows that the vast majority of the patients referred and included for the study came from ILD HPs (n=22 (88%) for FT, n=24 (83%) for WL) via either the outpatient clinic where I was regularly attending or via email. The vast majority (24 (96%) and 22 (92%) for FT and WL respectively were registered with a GP prior to recruitment. However, very few patients had either district nurse or community matron involvement prior to recruitment. Interestingly, more of the WL group had community respiratory nurse and community palliative care involvement prior to recruitment (community resp nurse FT n=2 (8%) vs WL 6 (25%) and CPCT FT n=1 (4%) vs WL 4 (17%)). The mean (range) time taken to set up the CC was 204 (60-360) mins in the FT group and 219 (60-390) mins in the WL group.

The mean length (range) of CC in the FT group was 94 (60-120) mins and in the WL group was 93 (60-150) mins. All patients in the WL group who received the CC had an informal caregiver who was also present at the CC. However only 19/25 patients who received the CC in the FT group had informal caregivers. 18/25 (72%) of these informal caregivers attended the FT CCs.

There was no difference in the HP attendance at either groups' CC. The majority of patients had at least 3 symptoms which needed to be addressed at the CC. The 2 main symptoms addressed were shortness of breath and cough. PPC was discussed in 17 (68%) of FT and 23 (96%) WL CCs. For 13 (52%) of FT and 23 (96%) of WL group this was home. PPD was discussed at 11 (28%) of FT and 10 (42%) of WL CC. Reasons for non-discussion for both PPC and PPD were patient choice. Implementation of the intervention in the 2 groups is compared in Table 5-3 Page 244 and Table 5-4 Page 245.

Table 5-3 Comparison of pre-CC demographics

	FT n=25	WL n=24
Referring profession n (%)		
ILD	22 (88%)	20 (83%)
Palliative Care	3 (12%)	4 (17%)
Referral mode		
via clinic	16 (64%)	15 (62%)
Via in-patient palliative care list	2 (8%)	3 (12%)
Via phone from ILD HP	0	2 (8%)
Via email from ILD HP	7 (28%)	4 (17%)
IP/OP		
IP	2 (8%)	3 (12%)
OP	23 (92%)	21 (88%)
H2H nurse		
DLL	6 (24%)	8 (33%)
CO	19 (76%)	16 (67%)
Registered with a GP prior to recruitment?		
Yes	24 (96%)	22 (92%)
No	1 (4%)	2 (8%)
District nursing team involved prior to recruitment?		
Yes	2 (8%)	3 (12%)
No	23 (92%)	21 (88%)
Community matron involved prior to recruitment?		
Yes	0	0
No	25 (100%)	24 (100%)
Community respiratory nurse involved prior to recruitment?		
Yes	2 (8%)	6 (25%)
No	23 (92%)	18 (75%)
CPCT involved prior to recruitment?		
Yes	1 (4%)	4 (17%)
No	24 (96%)	20 (83%)
Total time taken to set up CC in min		
Mean (SD)	204 (78)	219 (86)
Range	60-360	60-390

Table 5-4 Comparison of delivery of CC

	FT	WL
Length of CC (mins)		
Mean (SD)	94 (17)	93 (23)
Range	60 to 120	60 to 150
Median	90	90
Carer present at CC		
Yes	18 (72%)	24 (100%)
No	7 (28%)	0
Number of family members present at CC		
Mean	1.3	1.6
Mode	1	1
Range	0 to 6	1 to 4
Number of HP (excluding H2H CNS) at CC		
Mean	2.6	2.8
Mode	2	3
Range	1 to 6	1 to 4
GP present at CC		
Yes	8 (32%)	11 (46%)
No	17 (68%)	13 (54%)
District Nurse present at CC		
Yes	14 (56%)	19 (79%)
No	11 (44%)	5 (21%)
Community matron present at CC		
Yes	6 (24%)	4 (17%)
No	19 (76%)	20 (83%)
Community respiratory nurse present at CC		
Yes	5 (20%)	3 (12%)
No	20 (80%)	21 (88%)
CPCT present at CC		
Yes	19 (76%)	21 (88%)
No	6 (24%)	3 (12%)
Social Worker present at CC		
Yes	3 (12%)	0
No	22 (88%)	24 (100%)
Marie Curie present at CC		
Yes	1 (4%)	0
No	24 (96%)	24 (100%)
PPC discussed at CC		
Yes	17 (68%)	23 (96%)
No	8 (32%)	1 (4%)
Reasons for non-discussion		
Patient did not wish to discuss	8 (100%)	1 (100%)
PPC at CC		
Home	13 (52%)	23 (96%)
Hospital	4 (16%)	1 (4%)
PPD discussed at CC		
Yes	11 (28%)	10 (42%)
No	18 (72%)	14 (58%)
Reasons for non-discussion		
Patient did not want to discuss	18 (100%)	14 (100%)
PPD at CC		
Home	7 (64%)	5 (50%)
Hospital	0	0
Hospice	0	2 (20%)
Home/hospice	0	2 (20%)
Undecided at present	4 (36%)	1 (10%)

5.5.1.3 Missing data

Missing data is shown in Table 5-5 Page 246. As percentage of missing data for completed outcome measures is minimal and less than 5%, I have not used any imputation methods. Outcome data for completed (fully or partial) measures have been presented in section 5.5.1.4.

Unfortunately the VAS breathlessness scale was not completed appropriately. As a result, patients were classing their breathlessness on a 5 point Likert scale of none, slight, moderate, severe and extreme. Data for VAS has been presented as such.

Table 5-5 Amount of missing data for completed measures in the study, by time point for patient interviews

		Number of patients completing questionnaire	Total n items	N patients (%) with complete data	Total n missing items	% missing items
POS	Baseline	53	12	53	0	0
	Week 4	47	12	52	1	<1%
	Week 8	34	12	52	1	<1%
VAS	Baseline	53	1	53 (100%)	0	0
	Week 4	47	1	47 (100%)	0	0
	Week 8	34	1	34 (100%)	0	0
D12	Baseline	53	12	51 (96%)	9	1%
	Week 4	47	12	46 (98%)	5	<1%
	Week 8	34	12	33 (97%)	1	<1%
KBILD	Baseline	53	15	47 (89%)	6*	<1%
	Week 4	47	15	44 (94%)	7**	<1%
	Week 8	34	15	33 (87%)	1	<1%
MRC	Baseline	53	5	53 (100%)	0	0
	Week 4	47	5	47 (100%)	0	0
	Week 8	34	5	34 (100%)	0	0
SGRQ	Baseline	52***	50	29 (56%)	32^	1%
	Week 4	46	50	26 (57%)	31^	1%
	Week 8	33	50	22 (67%)	18^	1%
HADS	Baseline	53	14	53 (100%)	0	0
	Week 4	47	14	47 (100%)	0	0
	Week 8	34	14	34 (100%)	0	0

*5 patients missed the question “in the last 2 weeks, has your lung complaint made you feel fed up or down in the dumps?” ** 4 patients missed the question “in the last 2 weeks, has your lung complaint made you feel fed up or down in the dumps?” *** the first patient into the study completed the McGill quality of life questionnaire rather than SGRQ ^ The most commonly unanswered question was paid employment question with 20, 17 and 11 patients not answering in the baseline, week 4 and week 8 groups respectively.

The paid employment question is:

If you have ever had paid employment:

My chest trouble made me stop work altogether

My chest trouble interferes with my work or made me change my work

My chest trouble does not affect my work

Therefore if you have never worked or are retired, this question is not applicable to you. However, there isn't a N/A response. Therefore, it is possible that patients completing this part of the questionnaire may have left it blank as they couldn't find a N/A option

5.5.1.4 Outcomes

5.5.1.4.1 Primary endpoint data

There was a significantly greater reduction in total POS score between baseline and week 4 for the fast-track group than those in the waiting list group; mean change (SD) -5.7 (7.5) vs -0.4 (8.0) respectively. The mean change difference between the two arms was -5.3 (95% CI: -9.8 : -0.7) independent t test $p=0.02$; effect size (95%CI) of -0.7 (-1.2 to -0.1).

5.5.1.4.2 Secondary endpoint data

5.5.1.4.2.1 Patient data

The primary and secondary endpoint data is shown in Table 5-6 Page 249. The change in POS at week 4 in the FT group was sustained at 8 weeks. In addition, there was a reduction in POS scores between week 4 and week 8 (week 4 score (SD) 16.8 (8.9), week 8 score (SD) 12.5 (6.6)).

There was an improvement in the VAS breathlessness scores as time progressed in the FT group. Of note, there was no improvement in VAS scores between baseline and week 4 in the WL group but there was improvement between week 4 and week 8. There was no improvement in D12 scores in FT group but there was an improvement in D12 scores between week 4 and week 8 with a reduction of mean value (SD) at week 4 from 25.0 (10.7) to 21.3 (10.5) at week 8 in the WL group. There was no change in the MRC scores across both groups over time.

There was an improvement in patient QoL data with effect size (95% CI) of the intervention at 4 weeks of 0.6 (0.0 to 1.2) for KBILD. The KBILD score continued to improve in the FT group between weeks 4 and week 8 from 40.0 (16.2) to 43.2 (18.4). In addition, the KBILD score improved between week 4 and week 8 data collection in the WL group (30.3 (16.2) to 34.9 (18.0) respectively). For the SGRQ, there was an effect size of -1.0 (-1.6 to -0.4) at week 4 for SGRQ impact and -0.9 (-1.5 to -0.3) for SGRQ total. Of note, there were marked improvements in SGRQ symptoms (65.8 (23.0) vs 60.2 (23.8)), impact (74.8 (14.9) vs 62.3 (13.5)) and total scores (78.6 (11.8) vs 70.8 (10.8)) in the WL group between week 4 and week 8.

In addition there were positive effects on patient HADs scores with effect sizes (95% CI) for patient anxiety -0.6 (-1.1 to 0.0), patient depression -0.7 (-1.3 to -0.1), patient total HADs score -

0.7 (-1.2 to -0.1) at week 4. This effect appeared to be sustained in the FT group with continued improvement in scores at week 8. Of note, there was improvement from week 4 to week 8 in the WL group- Anxiety (10.8 (5.5) vs 7.9 (5.5)), Depression (12.3 (4.8) vs 9.3 (4.5)) and Total Score (23.0 (9.7) to 17.2 (9.4)).

5.5.1.4.2.2 Informal caregiver data

Effect size of the intervention on POS scores as reported by the informal caregiver at week 4 was -0.4 (-1.1 to 0.2). However, there was an improvement of POS scores in the WL group between week 4 and week 8 (18.0 (8.4) vs 13.7 (6.3)) respectively.

Effect size of intervention on ZBI at week 4 was -0.6 (-1.2 to 0.1). However, there was an improvement in ZBI scores between week 4 and week 8 in the WL group (31.7 (17.3) vs 25.4 (13.4)).

Effect sizes of intervention on informal caregiver depression and informal caregiver total HADs score were -0.7 (-1.3 to 0.0) and -0.7 (-1.3 to 0.0) respectively. Of note, there was improvement between week 4 and week 8 scores for the WL group for Anxiety (11.7 (5.6) vs 9.8 (4.6)), Depression (9.6 (4.9) vs 7.2 (3.9)) and Total Score (21.3 (9.9) vs 17.0 (8.2)).

There did not appear to be an effect of the intervention at week 4 on CQLC scores. However, there was improvement in score between week 4 and week 8 in the WL group: Burden (25.2 (8.5) vs 22.1 (9.2)), Disruptiveness (9.3 (5.5) vs (7.6 (5.9))), Financial (2.7 (2.8) vs 2.3 (2.1)) and Total Score (66.3 (18.4) vs 60.2 (23.9)).

5.5.1.4.2.3 Data related to study

Table 5-7 Page 250 shows quantitative outcomes measured after the CC. As of study close on 31/12/2013, a greater number of WL patients had died than FT: FT 8 (32%) vs 13 (54%). There appeared to be a similar length of time from randomisation to death for both groups. PPC and PPD was achieved in lower percentages of patients who died in the WL group; PPC: FT 8 (100%) vs WL 11 (84%), PPD: FT 7 (88%) vs WL 10 (77%). A larger percentage of patients died at home in the FT group; FT 5 (62%) vs WL 5 (38%) and in hospital in the WL group; FT 1 (12%) vs WL 5 (38%). All 3 patients who died before being able to receive the CC were in the WL group and all died in hospital.

Table 5-6 Table showing primary and secondary endpoint data for patients and informal caregivers

	FT				WL				Effect size (95% CI) at 4 weeks
	Baseline (mean (SD) or n(%))	4 weeks (mean (SD) or n (%))	Change score Mean (SD)	8 week (mean(SD) or n(%))	Baseline (mean (SD) or n (%))	4 weeks (mean (SD) or n (%))	Change score Mean (SD)	8 week (mean(SD) or n(%))	
Primary endpoint	N=26	N=23			N=27	N=24			
POS	16.8 (5.6)	11.2 (7.9)	-5.7 (7.5)		17.0 (6.3)	16.8 (8.9)	-0.4 (8.0)		-0.7 (-1.2 to -0.1)
	The mean change difference between the two arms was -5.3 (95% CI: -9.8 : -0.7) Independent t test p=0.02								
Secondary endpoint									
Patients									
POS				N=19				N=15	
				11.2 (7.3)				12.5 (6.6)	
VAS	N=26	N=23		N=19	N=27	N=24		N=15	
None	0	0		0	0	0		0	
Slight	0	2 (9%)		4 (21%)	0	0		2 (13%)	
Moderate	15 (58%)	15 (65%)		11 (58%)	8 (30%)	8 (33%)		10 (67%)	
Severe	11 (42%)	6 (26%)		4 (21%)	19 (70%)	16 (67%)		3 (20%)	
Extreme	0	0		0	0	0		0	
D12	N=25*	N=22*		N=19	N=27	N=24		N=15	
	22.8 (8.7)	21.6 (10.1)	-0.8 (7.2)	20.4 (9.8)	25.9 (8.2)	25.0 (10.7)	-0.6 (21.3)	21.3 (10.5)	-0.3 (-0.9 to 0.3)
KBILD†	N=26	N=23		N=19	N=27	N=24		N=15	
	35.8 (13.0)	40.0 (16.2)	3.5 (11.0)	43.2 (18.4)	32.3 (12.9)	30.3 (16.2)	-2.6 (21.3)	34.9 (18.0)	0.6 (0.0 to 1.2)
SGRQ	N=25**	N=22**		N=18**	N=26***	N=24		N=15	
symptoms	62.2 (17.7)	62.0 (20.5)	1.4 (16.5)	52 (20.1)	66.3 (24.5)	65.8 (23.0)	-2.0 (23.7)	60.2 (23.8)	-0.2 (-0.8 to 0.4)
activity	88.9 (9.7)	85.3 (17.6)	-3.1 (13.6)	87.1 (10.7)	93.7 (5.0)	92.4 (7.8)	-1.6 (6.8)	91.4 (5.2)	-0.5 (-1.1 to 0.1)
impact	61.6 (18.0)	56.3 (20.3)	-4.0 (19.7)	57.4 (20.8)	71.4 (12.8)	74.8 (14.9)	2.8 (13.3)	62.3 (13.5)	-1.0 (-1.6 to -0.4)
total	70.0 (13.0)	66.0 (16.4)	-2.8(14.9)	65.7 (14.7)	76.8 (10.1)	78.6 (11.8)	0.7 (10.5)	70.8 (10.8)	-0.9 (-1.5 to -0.3)
PPS†	N=26	N=23		N=19	N=27	N=24		N=15	
Median	60	60		60	60	60		60	
IQR (25-75)	50-60	50-60		60-70	50-60	50-60		60-70	
MRC	N=26	N=23		N=19	N=27	N=24		N=15	
Median	4	4		4	5	5		4	
IQR (25-75)	4-5	4-5		4-5	4-5	4-5		4-5	
HADs	N=26	N=23		N=19	N=27	N=24		N=15	
Anxiety	9.6 (4.6)	8.1 (4.1)	-1.7 (3.3)	7.1 (4.6)	9.7 (5.7)	10.8 (5.5)	1.2 (4.8)	7.9 (5.5)	-0.6 (-1.1 to 0.0)
Depression	9.0 (3.1)	9.4 (3.0)	0.3 (3.2)	8.3 (3.7)	11.0 (4.7)	12.3 (4.8)	1.5 (4.12)	9.3 (4.5)	-0.7 (-1.3 to -0.1)
Total Score	18.6 (6.4)	17.5 (6.3)	-1.4 (5.0)	15.4 (7.7)	20.7 (9.0)	23.0 (9.7)	2.8 (8.1)	17.2 (9.4)	-0.7 (-1.2 to -0.1)
Carers									
POS	N=19	N=15		N=13	N=26	N=22		N=15	
	17.8 (6.5)	14.7 (6.5)	-2.9 (5.8)	16.1 (6.9)	18.5 (6.2)	18.0 (8.4)	-0.7 (9.6)	13.7 (6.3)	-0.4 (-1.1 to 0.2)
ZBI	N=19	N=16		N=13	N=26	N=23		N=16	
	22.2 (15.2)	22.3 (15.3)	0.1 (0.2)	26.2 (13.4)	32.2 (11.7)	31.7 (17.3)	-0.1(0.3)	25.4 (13.4)	-0.6 (-1.2 to 0.1)
HADS	N=19	N=16		N=13	N=26	N=23		N=16	
Anxiety	9.3 (4.3)	8.8 (4.8)	-0.5 (4.8)	9.2 (3.7)	11.0 (5.9)	11.7 (5.6)	0.6 (5.3)	9.8 (4.6)	-0.6 (-1.2 to 0.1)
Depression	7.0 (4.9)	6.4 (4.1)	-0.3 (3.5)	7.0 (4.2)	8.7 (5.0)	9.6 (4.9)	1.0 (4.6)	7.2 (3.9)	-0.7 (-1.3 to 0.0)
Total Score	16.3 (8.7)	15.2 (8.3)	-0.8 (8.0)	16.2 (7.4)	19.7 (10.4)	21.3 (9.9)	1.7 (8.7)	17.0 (8.2)	-0.7 (-1.3 to 0.0)
CQLC†	N=18	N=15		N=13	N=25	N=21		N=13	
Burden	21.9 (8.3)	21.5 (7.1)	-0.6 (6.9)	20.2 (5.7)	25.2 (8.3)	25.2 (8.5)	-0.2 (8.0)	22.1 (9.2)	-0.5 (-1.1 to 0.2)
Disruptiveness	7.8 (6.0)	7.1 (6.9)	-0.6 (4.3)	7.7 (4.8)	9.6 (5.4)	9.3 (5.5)	0.0 (4.9)	7.6 (5.9)	-0.4 (-1.0 to 0.3)
Adaptation	15.6 (5.1)	15.8 (6.1)	0.5 (4.3)	15.9 (5.4)	14.7 (6.8)	14.4 (5.7)	0.1 (5.3)	16.8 (4.2)	0.2 (-0.4 to 0.9)
Financial	2.8 (3.0)	2.5 (3.0)	-0.4 (2.1)	2.4 (3.6)	2.7 (2.9)	2.7 (2.8)	0.3 (2.5)	2.3 (2.1)	-0.1 (-0.7 to 0.6)
Total Score	60.8 (17.4)	58.5 (15.3)	-2.5 (11.0)	58.3 (15.6)	66.7 (16.3)	66.3 (18.4)	0.7 (15.2)	60.2 (23.9)	-0.4 (-1.1 to 0.2)

*1 patient had greater than 3 items missing on the D12 questionnaire and was therefore excluded as per author's instructions. , ** 1 patient completed McGill quality of life not SGRQ, *** 1 patient removed as greater than 6 items missing on activity SGRQ. † Increase in scores indicates improvement

Table 5-7 Comparison of post CC outcomes

	FT	WL
Number of deaths of patients who received CC (as of study close on 31/12/2013)	8 (32%)	13 (54%)
Number of days from CC to death	n=8	n=13
Mean (SD)	168 (106)	139 (129)
Range	18 to 368	21 to 420
Number of days in PPC		
Mean (SD)	166 (103)	133 (134)
Range	18 to 358	0 to 419
PPC achieved		
Yes	8 (100%)	11 (84%)
No	0	2 (16%)
PPD achieved (NB PPD changed for some patients after CC)	n=8	n=13
Yes	7 (88%)	12 (92%)
No	1 (12%)	1 (8%)
Actual place of death	n=8	n=13
Home	5 (62%)	5 (38%)
Hospital	1 (12%)	5 (38%)
Hospice	2 (25%)	3 (23%)
Place of death of those who died before receiving CC	n=0	n=3
Home	0	0
Hospital	0	3 (100%)
Hospice	0	0
H2H contacts in addition to scheduled follow up (min)		
Mean (SD)	48.8 (77.5)	35.0 (48.1)
Range	0-300	0-120

5.5.2 Qualitative findings

Qualitative findings are presented in Appendix 2 of the published paper.

5.5.3 Feasibility

1. Did the feasibility/pilot study allow a sample size calculation for the main trial?

The sample size calculation for an Evaluation trial is based on using the population variance of the POS.(216) This is estimated by means of the common standard deviation from the phase II study which is 8.456. Conventional multiplier for alpha=0.05 and conventional multiplier for power=0.80. (216)

$$N=2[(1.96+0.842)^2 * 8.456^2 / (16.8-11.2)^2]$$

$$N=2(7.8*79.21)/31.4$$

$$N=37 \text{ per group}$$

2. What factors influenced eligibility and what proportion of those approached were eligible?

The main factor which influenced eligibility was diagnosis. Patients were referred to the study who did have an ILD diagnosis but were not IPF or NSIP patients. These patients were therefore excluded from the study on diagnosis. 82/120 patients who were approached were eligible.

3. Was recruitment successful?

Recruitment was successful. There were a number of barriers to recruitment as discussed in section 5.6 but these were not related to problems within the trial and would not be applicable if the trial were to be repeated.

4. Did eligible participants consent?

There were 82 patients eligible to participate in the trial (120 patients were referred for the trial and 38 did not meet inclusion criteria). 15/82 of these patients died before they could be approached to take part in the trial. Of the remaining 67 patients, 53 consented to be included with 14 declining to participate. Therefore 79% of patients eligible to take part in the trial that were approached, consented.

5. Were participants successfully randomised and did randomisation yield equality in groups?

Randomisation yielded equality in clinical parameters and POS scores for which the patients were stratified. However, more patients in the FT group had informal caregivers than in the WL group.

6. Were blinding procedures adequate?

No blinding.

7. Did participants adhere to the intervention?

The patients adhered to the intervention but they did not adhere to the study protocol at all times. Principally, this related to patients and informal caregivers no longer returning questionnaires once they had received the CC. This is discussed further in section 5.6.

8. Was the intervention acceptable to the participants?

The intervention of the CC was acceptable to participants.

9. Was it possible to calculate intervention costs and duration?

Cost was not calculated but would need to be done for any future studies. Length of CC and input needed from the H2H CNS after delivery of the intervention were recorded. If needed approximate costs of delivering the intervention may be calculated to assess feasibility of delivering the intervention from a cost perspective.

10. Were outcome assessments completed?

Questionnaires were more likely to not be completed once the patient had received the intervention. The questionnaires could be simplified or they could be completed by a researcher visiting the patient/informal caregiver to try to alleviate some of the burden. This is discussed further in section 5.6

11. Were outcomes measured those that were the most appropriate outcomes?

There are limited palliative care outcomes which have been validated in this group. In particular, there are no validated outcomes in the informal caregiver group. The outcomes measured

appear to be appropriate. However, it may be valuable to have a greater number of detailed symptom control outcomes which may fully capture any changes to other symptoms such as cough. A potential outcome measure which could be used is the Leicester Cough Questionnaire which has been validated in ILD.

12. Was retention to the study good?

Please see section 5.5.4

13. Were the logistics of running a multicentre trial assessed?

No- this was not a multi-centred trial.

14. Did all components of the protocol work together?

All components of the protocol did work together. However, there were difficulties in ensuring that the intervention was delivered when it was supposed to be and outcomes measures completed in a timely manner.

The original criteria set for feasibility were:

- Consent rate at least 25%
- Recruitment of 52 patients
- 80% of patients in the FT group were able to receive the H2H intervention within 14 days of their allotted time.

The first two points were achieved. However, the final point was not. This will be discussed further in the next section.

5.5.4 Acceptability

5.5.4.1 Recruitment, follow up and attrition

Patients were recruited for the phase II trial from October 2011 to October 2013 and followed up until study close December 2013 when place of death was documented if applicable.

It was difficult to get participants to return questionnaires at exact time points of 4 weeks and 8 weeks. In addition, it was also difficult at times to get the CC arranged for within one week (for FT) or just after 4 weeks (for WL). It was not possible to get 80% of the FT group to have their CC within 14 days from randomisation. Therefore, if needed the week 4 and subsequent week 8 assessments were delayed. Exact timings of interventions and assessment points for the 2 groups are shown in Table 5-8 Page 254.

Table 5-8 Table to show timings of CC and follow up

	FT	WL
Time from baseline questionnaire to CC (days)	n=25	n=24
Median	23	40
Range	12 to 51	7 to 100
Number of patients having CC within 14 days of randomisation	6 (24%)	N/A
Reasons for delay in CC if any		
Difficulty finding convenient date for HP	19	7
Difficulty finding convenient date for patient or family		1
Time from CC to 4 week questionnaire (days)	n=23	n=24
Median	19	-1
Range	-4 to 35	-11 to 38
Time from week 4 to week 8 questionnaire (days)	n=19	n=15
Median	28	29
Range	20 to 49	7 to 69

Reasons for loss to follow up included attrition due to death (ADD) FT 1, WL 6, attrition due to illness (ADI) FT 0, WL 1 and attrition at random (AAR) FT 2 and WL 0 (see Table 5-9 Page 255)

Table 5-9 Table to show reasons for attrition

	FT			WL		
	Baseline	Week 4	Week 8	Baseline	Week 4	Week 8
ADD	0	1	0	0	3	3
ADI	0	0	0	0	0	1
AAR	0	1**	1***	0	0	0
Other	0	1	3*	0	0	4*

*Patients were less likely to return their questionnaires that they completed themselves once they had received the H2H CC. This was despite follow up reminder phone calls. They were however contactable via phone. ** lost to follow up- went abroad on holiday *** lost to follow up- went abroad for transplant assessment

5.5.4.2 Qualitative acceptability findings

5.5.4.2.1 Timing

The timing of the intervention was thought to be appropriate and the earlier in the disease process it occurred, the more perceived benefit there was:

“it is (1) better (3) than (3) later you know if all these things happen once you’re bed ridden (2) erm (3) you know you’ve got people coming in (2) that you don’t know at least you know this way I mean we know::w the nurses...you know we know them first name terms erm you know you you feel comfortable with them erm (5) you know I do think it’s definitely it nee- it needs to be done that way erm and that much earlier.” (Leslie, 54 year old wife of Ted who had advanced IPF).

The length of questionnaires was deemed to be acceptable. In addition, the interval between questionnaires was also deemed to be appropriate; a 4 week interval between questionnaires was felt to be adequate to capture any changes in symptom control or quality of life. In addition, the questionnaires used were also felt to assess change satisfactorily by patients, informal caregivers and HPs with the right outcome measures being used. One patient (Alfred) had felt that there was some repetition between questions in outcome measures and had become confused at times as some measures had asked about experiences over last 3 days (POS) and others over last 2 weeks (SGRQ).

Patients and informal caregivers alike did not feel that the questionnaires caused distress. There was a recognition that questions about death and dying were necessary but patients and informal caregivers alike did not feel that these caused suffering.

5.5.4.2.2 Evidence based guidelines

At the CC, patients and informal caregivers as well as the HPs were given the evidence based guidelines. Both patients and informal caregivers were grateful for the guidelines (even though they weren't specifically tailored to the lay person). Patients such as Alfred felt that they encouraged him to research areas that were not familiar but found it encouraging that he was using the right things in other areas.

All HPs were extremely grateful for the guidelines. For example, the ILD Consultant found them very useful and he felt they allowed systematic evidence based symptom control rather than ad hoc delivery of symptom control as he had previously done. Generalists such as the GP found them invaluable and specifically appreciated having guidance from specialists which again reassured him and instilled confidence that he was doing the right thing and guided him on aspects of symptom control he wasn't sure about.

5.5.4.2.3 Fast Track design

Patients and informal caregivers interviewed did not feel that there was any problem with the FT design. One informal caregiver in particular (Penny, wife of a 67 year old patient with IPF) did not feel it was significant to have to wait one month for the intervention as she did not feel that her husband's prognosis was so short that waiting would matter. However, the Community palliative care CNS did feel that it mattered especially if a patient was particularly unwell, she felt the wait could affect the care:

"I do think with some of them that it would cause problems. Erm I think that it would have been too late particularly if they're very poorly.... and you can't necessarily predict that with everybody and actually some of them (1) 4 weeks (2) would be too much without all that help...." Community Palliative Care CNS

However, there was an understanding from those with a research background such as the ILD Consultant that 4 weeks was a reasonable time period for the WL group to wait before receiving the intervention as it often took longer than that to set up support in the community.

5.5.4.2.4 Positive comments

All patients and informal caregivers interviewed were grateful for having taken part in the study:

“...just to say I'd like to thank you erm (1) for giving me the opportunity to go on this in- like on this survey [study] and to get the help that I've I've now got I really do appreciate it.....” (Peter, 63 year old with advanced IPF).

“I think the study's excellent” (Stephen, a 81 year old patient with NSIP)

In addition, HPs also felt extremely positive about the CC and reported that patients and informal caregivers had fed back to them about their experience:

“we've had good (1) er quite a lot of good feedback from patients as well that it's been very useful for them with regards to symptom management and having someone coordinate their overall care” ILD Consultant

“on every level I found it very very (3) er::: (4) useful.....I think it's brilliant...” GP

Overall patient participants were extremely positive about the intervention and in particular the CC which they had found excellent, well organised and incredibly useful. Patients and informal caregiver participants felt that the CC “*laid everything on the table*” and importantly improved quality of life as it addressed concerns and anxieties that had been playing on patients' and informal caregivers' minds. Patient and informal caregiver participants felt that the intervention had been delivered in a “*very compassionate and understanding way*” where all the patients' and informal caregivers' concerns were acknowledged and addressed. Patient participants appreciated that the CC was in their home with all the HPs involved in their care in the same place at the same time making patients and informal caregivers feel “*important*” –what was imperative is that this allowed patients' and informal caregivers' concerns to be addressed on their terms. Patient participants thought it important that HPs had a clear understanding of the environment they lived in on a day to day basis and conducting the CC in the patient's home facilitated this.

5.5.4.2.5 Harms

There were very few if any negative comments related to the intervention; even though the nature of palliative care involvement had been clearly communicated with the patient and informal caregiver involved in the study, in one instance another family member had become upset when attending the CC to see that the local hospice team were attending. In addition, one informal caregiver had initially felt upset when their loved one had discussed PPC and PPD at the CC but on reflection, they realised how important having the conversation at that point had been. One patient in the WL group did not feel there was any point to the CC and he did not feel that he had gained anything from it.

5.6 Discussion

This mixed methods Fast-track RCT trialed the H2H intervention in PIF-ILD patients and informal caregivers. This trial has provided valuable information on possible effects of the intervention on the palliative care needs of patients and informal caregivers in this group, whilst showing the intervention to be largely feasible and acceptable.

I will now discuss the main findings from this trial in relation to the main aims followed by limitations and implications for clinical practice.

5.6.1 Aim 1- To begin to evaluate H2H in a phase II study

This Fast-track RCT of a case conference intervention in advanced fibrotic ILD patients and carers identified an improvement in both symptom control and quality of life. Of note, there was no worsening of any outcome after receiving the intervention. This suggests that no harm and potentially a prevention of deterioration may have occurred. The quantitative results showed a positive and significant effect on patients' POS scores at the primary endpoint of 4 weeks with a mean change score of 5.7 points in the FT group which was sustained at 8 weeks. In addition, there was improvement in the WL POS score between week 4 and week 8 of 4.3 points. For the POS, a variation of one point in individual items is linked to clinical meaningful change.(161) This suggests that the H2H intervention may improve the palliative care needs of PIF-ILD patients in a clinically meaningful way. The 2 RCTs that have previously trialed CCs in the cancer setting (78, 80) have not used the POS or a global palliative care assessment tool so a direct comparison cannot be made on effectiveness in the PIF-ILD setting.

At the CC, the evidence based guidelines were used and a comprehensive palliative care assessment (including symptom control, psychological, social needs and crisis management plan) was carried out. Ongoing management of the patients' palliative care needs were carried out by the community teams. It is possible that the intervention of the evidence based guidelines and the ongoing management of the palliative care needs identified at the CC, resulted in the improvements in the patients' POS seen. It is difficult to know whether the benefit from the intervention seen is due to the CC, palliative care involvement or the added time with care providers. However, the results are promising and warrant further investigation.

Of note, the WL group had a higher percentage of informal caregivers. Informal caregivers play a vital role in the management of symptoms in the home setting.(217) In addition, HPs providing palliative care in the community setting report that they rely on informal caregivers' assessments of the patients' condition and use them as cues for action.(217) Therefore it may be expected that if a patient does not have an informal caregiver, this interface is more difficult potentially leading to more unmet palliative care needs. The WL group also had a higher GP, DN and CPCT presence at the CC than the FT group. This may have influenced outcomes. Palliative care teams have been shown to positively influence patient and informal caregiver outcomes (218) and it would usually be the GP, district nurses and CPCT who would instigate the symptom control interventions and manage the patients' palliative care needs on a day to day basis. The higher presence of these HPs at the WL CC may have led to false improvements in the WL scores which would only have diluted the effect size, suggesting that the potential effect of the intervention may be greater than reflected in the primary outcome.

Baseline scores showed that patients were living with poor QoL. There was an improvement in QoL scores on both the KBILD and SGRQ impact and total scores at week 4 in the FT group. The improvement in the WL SGRQ impact and total scores were marked between week 4 and week 8 where both domains showed improvement greater than the Minimal Important Clinical Difference (MID) for IPF. Mitchell et al (78) investigated the impact of a telephone CC between GPs and specialist palliative care teams (without the patient or informal caregiver present) in a RCT of 159 cancer patients in Australia. They found that the primary outcome- global QoL was not influenced by the intervention but the CC group showed better maintenance of physical and mental health measures of QoL in the 35 days before death. The authors suggest this is because care plans at referral were not implemented until severe symptoms developed. However, the Mitchell et al study was a CC to meet professional needs, whilst the H2H service was a patient-centred, face-to-face intervention involving, patients, informal caregivers and HPs. This may have been an influencing factor. The QoL measures used in the Mitchell et al study were the Assessment of Quality of Life at the end of Life (AQEL) (219), the McGill Quality of Life Questionnaire (220) and the Subjective Wellbeing Scale (221) so direct comparisons between the two studies are not possible. Interestingly, the complex intervention of a breathlessness intervention service delivered by Higginson et al study (222) also showed some improvements in QoL domains. The Higginson et al study is a RCT of 105 patients with refractory

breathlessness which included ILD patients. It found that the patients who received the integrated palliative care and respiratory breathlessness support service had, at 6 weeks, significantly improved breathlessness mastery, a domain of the Chronic Respiratory Disease Questionnaire. Mastery assessed patients' feeling of control over their breathlessness and its effects on QoL and function, and was on average 16% higher for those patients receiving the breathlessness support service. However, numbers of ILD patients were small 19 (18%) and ILD patients' diagnoses were not differentiated.

Improvements were also identified in anxiety and depression scores. Of note, baseline mean patient anxiety and depression scores and mean carer anxiety scores in both groups were borderline abnormal or abnormal. Subsequently, there were improvements in anxiety and depression scores of both patients and informal caregivers at week 4 in the FT group. This effect appeared to be sustained with continued improvement in scores at week 8. Importantly, the WL group showed deterioration for all anxiety and depression scores in both the patients and informal caregivers during the 4 week wait. Scores subsequently improved after the WL group received the intervention-improvements in HADs scores seen were greater than the MID (1.5) for COPD. Even though the HADs has not been validated in IPF, the MID for COPD has been used previously for IPF patients.(223) Lindell et al (113) conducted a mixed methods RCT of 21 patients looking at a disease management program delivered using a format of support group for both IPF patients and informal caregivers with a control group of best usual care. They found on quantitative analysis, that there was an increase in anxiety scores and decrease in QoL scores in the intervention group. In contrast, the qualitative work indicated that patients did not feel isolated and felt the intervention had enabled them to put the disease into perspective, gave comfort and provided an improved mental picture. In the Higginson et al study (222) breathlessness intervention service trial, there were also non-significant improvements in depression. The quantitative and qualitative results in the H2H trial were in agreement. In addition, the effect on anxiety and depression scores seen in patient scores were mirrored in the informal caregiver results with improvements in the depression and total HADs scores at week 4 in the FT group and improvements (greater than the MID) in the WL group between week 4 and week 8 in all 3 domains of the HADs.

Improvements were seen in the ZBI and CQLC between week 4 and week 8 in the WL group. In the Mitchell et al study(78), there was a positive impact on caregiver burden with significantly lower carer burden in two of the five domains (impact on schedule and lack of family support) on the Caregiver Reaction Assessment (79) as well as the total score. Knowing what to monitor, how to interpret the signs successfully and when to inform a HP were all issues of concern for informal caregivers in a previous palliative care study.(217) In the H2H trial, a copy of the individualised care plan made at the CC was given to the patient, informal caregiver and HPs involved in the care of the patient. This included direct contact numbers for all HPs and step-wise instructions of what to do in the event of deterioration. Patients, informal caregivers and HPs reflected in the qualitative interviews that they were very grateful for this individualised care plan with patients and informal caregivers expressing that this greatly reduced their anxiety and HPs expressing that it allowed them to provide better care. In addition, the qualitative data suggests that the intervention facilitated improvement in both the co-ordination and efficiency of care delivered with patients and informal caregivers expressing that they now felt that they were “*fast-tracked*” through the system as HPs had been made aware of the seriousness of their condition. Qualitative results suggest that this resulted in patients and informal caregivers being able to access help when needed. The actual process of the CC, having a clear individualised care plan and being supported in this way by the community HPs may have helped to reduce both patients’ and informal caregivers’ anxieties seen in the quantitative results.

The H2H intervention aimed to manage uncertainty by facilitating early discussion about disease progression, improving communication and addressing end of life planning needs. At the CC, not all patients wanted to talk about advance care planning decisions such as PPC and PPD. This was also found in the cluster randomised study conducted by Abernethy et al (80) where prognosis, end of life issues and previous experiences of death and dying were rarely discussed at the CC for cancer patients. For those patients who did discuss advance care planning at the H2H CC, even though it could initially be distressing for relatives present, it was seen as incredibly useful. For some patients, the CC gave permission to conduct these important conversations. Interestingly, many patients who had not wanted to discuss these issues at the CC, then went on to have subsequent discussions with their community HPs in the weeks after the CC. This may have been precipitated by the initial discussions by the H2H

nurse and the development of relationships with the community palliative care team after the case conference. This is in itself an important influence that the intervention may have had.

A diagrammatic representation of the possible effects of the H2H intervention is shown in Figure 5-9 Page 264 .

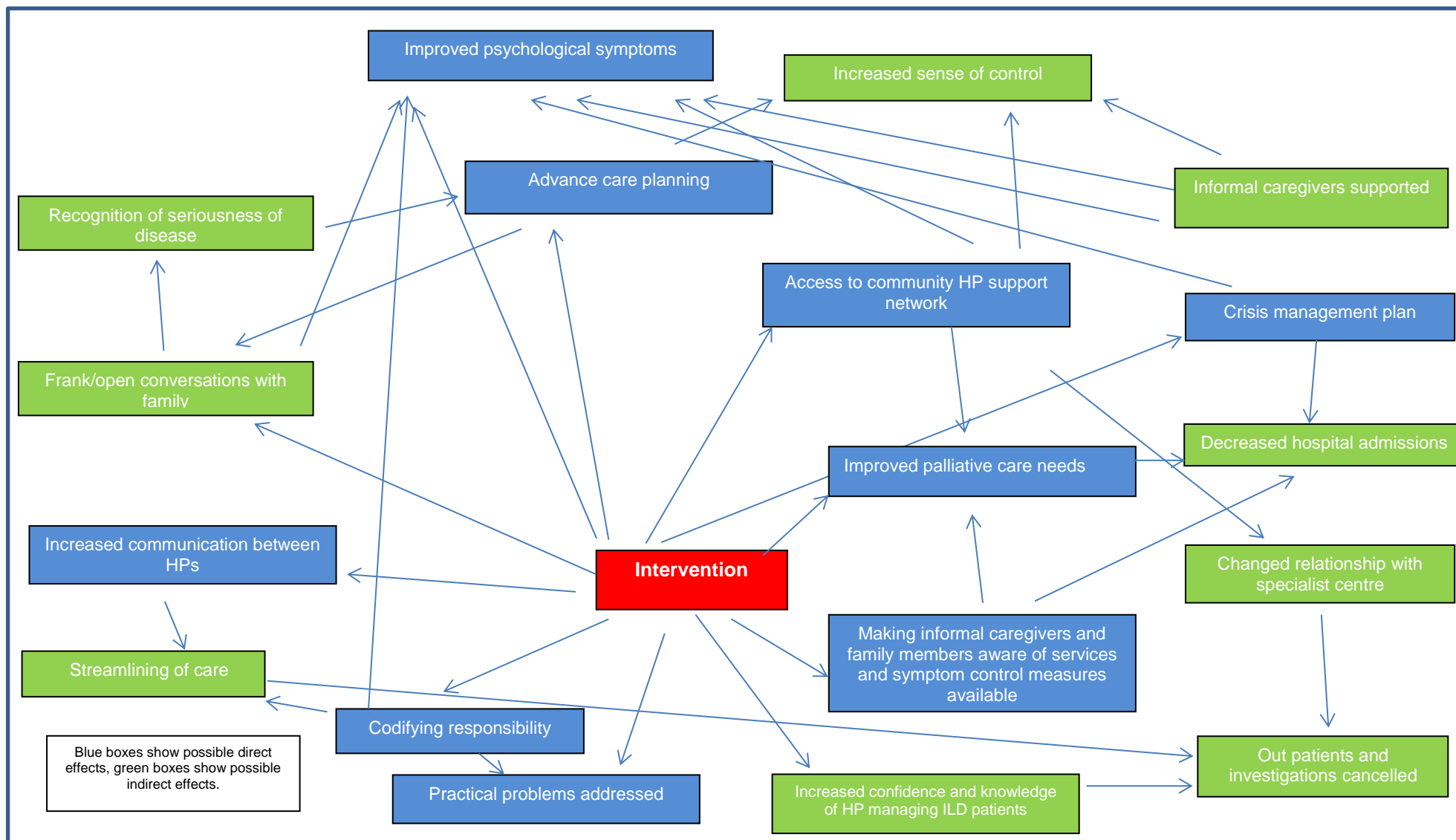


Figure 5-9 Figure to show possible mechanism by which H2H may be effective

3 of the WL patients died before receiving the CC. All 3 of these patients died in hospital. During the CC, for patients who wished to discuss PPD, no patient expressed hospital as their PPD. The actual place of death for patients having received the CC was hospital in only 28% of patients. This is much less than found in the retrospective case note review in Chapter 1 which found that 76% of PIF-ILD patients attending RBH and KCH died in the acute hospital setting. It has been noted in the literature that patients with IPF experience increased healthcare resource utilisation, and direct medical costs.(224) This is especially important at the end of life. It is possible that the CC, through establishing links in the community setting and preventing crisis admissions, enabled patients to not die in hospital. The extent of the economic benefit of this needs to be further investigated. Interestingly in the Abernethy et al trial (80), patients who lived the longest derived the most benefit in terms of better maintained performance status and fewer hospitalisations, supporting early referral to palliative care. The qualitative work in this trial showed that during the trial, patients became less likely to return to the specialist centre for investigations and out-patient appointments. This may be because as community HPs gained confidence in delivering care to these patients and patients' confidence in HPs ability to deliver this care grew, patients felt less reliant on the specialist centre and became less likely to return to the specialist centre. The qualitative findings indicated that there was recognition from patients and informal caregivers that the palliative care needs of these patients were best delivered in the community setting but patients and informal caregivers hadn't previously been able to access this support and there hadn't been confidence in the community teams to deliver care.

5.6.2 **Aim 2- To evaluate H2H in terms of feasibility and acceptability in a phase II study**

5.6.2.1 **Attrition and missing data**

Attrition is defined as the loss of patients from the study. A suggested taxonomy is attrition due to death (ADD), attrition due to illness (ADI) and attrition at random (AAR).(121) In this trial there was attrition of 3 patients between baseline and week 4 in the FT group and baseline and week 4 in the WL group. For all the patients in the WL group, this was ADD. In addition, there was attrition of patients who having received the intervention, did not complete and return their questionnaires. There were 3 patients in the FT group and 4 in the WL group this applied to. The patients were still contactable via phone and were not unwell. The qualitative interviews suggest that the questionnaires were not too burdensome. It is possible that after receiving the CC, participants did not feel motivated to return the questionnaires.

Missing data can more generally be defined as the absence of parts of patient's data.(121) Rubin's classification defines three types(225): missing at random (MAR) when missingness may depend on single variables, completely missing at random (CMAR) when missingness is not related to the specified variables and missing not at random (MNAR). For data in this study, the data is likely to be MNAR. The questions in the KBILD which were most likely not to be answered related to low mood and were consistent between questions. The most commonly unanswered question on the SGRQ was related to paid employment which was not applicable if you were retired. As there was no "not applicable" option, participants would have been likely to leave this blank if it did not apply to them. The average age for both the FT and WL groups was greater than 65 years, even though employment status was not collected in the demographic information, it is likely that a significant proportion of the patients would have been retired.

5.6.2.2 **Feasibility of trial**

Patients and informal caregivers when interviewed did not have any concerns with the FT design. However, there were some concerns expressed by a community HP who felt that 4 weeks was an unreasonable time period to wait if a patient was unwell and in need of community support. Only 10% of patients receiving CCs had CPCT involvement prior to referral

to the trial. Through the trial, the remainder of these patients were referred. The lack of referral appears to be due to a lack of recognition by HPs of the palliative care needs of these patients. These patients would therefore have been unlikely to have received any community support if they had not been recruited to the trial. In addition, the waiting period of 4 weeks used in this trial would equate to a normal wait within the NHS for referral to community services. Even though patients in the WL group did not receive the CC until after 4 weeks, referrals to community services were made at randomisation. A number of these community services were then making contact (and sometimes visiting) with the patients and informal caregivers before the CC- it is unclear for how many WL patients this was the case. This is likely to have affected and potentially diluted the effect size of the intervention at the primary end point of 4 weeks. Over three quarter (79%) of patients eligible to take part in the trial that I approached consented to participate. In a very few instances, patients who were suitable for the trial refused to take part. On feedback, they expressed that they were not quite ready to “accept they were palliative”. In these instances I encouraged patients to keep the information sheet and contact me if they changed their mind. However, I did not feel it ethical to approach them again. The qualitative work observed that patients, informal caregivers and HPs had misconceptions of what palliative care and its role represented. This finding has been observed elsewhere (226) among cancer patients. As palliative care becomes more prominent in managing the symptoms of ILD patients and becomes involved in the disease journey at an earlier stage, perhaps these misconceptions will change.

Randomisation yielded equality in clinical parameters and POS scores. However, more patients in the FT group had informal caregivers than in the WL group and this may have been an influencing factor (as discussed previously).

The timing of the intervention was thought to be appropriate with patients and informal caregivers appreciating the benefit of conducting the CC before the patient entered the terminal stages of the disease.

Importantly all information, including time points, about who received the H2H intervention is clearly presented. This has been highlighted as important when assessing the feasibility and fidelity of complex intervention trials in healthcare. (227)

5.6.2.3 Feasibility of assessments

Patients and informal caregivers alike did not feel that the questionnaires caused distress. There was a recognition that questions about death and dying were necessary but patients and informal caregivers alike did not feel that these caused suffering. There were 3 patients in the FT group and 4 in the WL group who received their CC and did not return subsequent questionnaires. The patient representative on the Project Advisory Group and the qualitative interviews suggest that the questionnaires were not too burdensome. It is possible that after receiving the CC, participants did not feel motivated to return the questionnaires. The questionnaires were postal and were reliant on the patient completing and posting them back.

An amendment to the wording on the patient and informal caregiver information sheet was submitted and approved. This removed suggestion that “care is being transferred from the hospital setting to the community”. Feedback from patients and informal caregivers had indicated that this was perceived negatively by patients and informal caregivers and as a result may have affected recruitment. This is likely to be due to the reliance that patients and informal caregivers placed on the specialist centre before involvement in the trial and was reflected in the qualitative findings.

Both the length and interval between questionnaires was deemed acceptable. The outcomes used were felt to capture and assess change satisfactorily for both symptom control and QoL. There are limited palliative care outcomes which have been validated in this group. The outcomes measured appear to be appropriate. One patient did find the varied time periods measured in each outcome confusing. In addition, it may have been valuable to have a greater number of detailed symptom control outcomes for other significant symptoms such as cough.

5.6.2.4 Feasibility of the intervention

Patients, informal caregivers and HPs alike praised the CC model of care. In previous qualitative work following the Mitchell et al RCT, GPs reported that the CC allowed them to be better informed, made discharge planning easier and allowed clear delineation of role between the GP and the palliative care service.⁽⁷⁶⁾ All of these findings were supported in this trial and the qualitative results supported feasibility of the intervention. In addition, there was adherence to the intervention (completion of the CC and follow up phone contacts). However, there was

some “gatekeeping” within the ILD department when patients were identified as possibly suitable for the trial. There had been very little communication within the ILD department at RBH with patients about end of life issues before commencement of the trial. Therefore some patients were not referred to the trial by the ILD HPs to “*protect the patients*” from end of life discussions which would occur as part of the intervention. A recent qualitative study exploring how transitions to a palliative care approach are perceived to be managed in acute hospital settings in England observed that health professionals believed achieving consensus among the clinical team about transition to palliative care was fundamental to the transition being effected.(228) I gently encouraged HPs to refer and questioned them in clinic. However, I believe the most effective tool in negotiating this barrier was the positive feedback from patients and informal caregivers who had already participated in the study who returned to the ILD out-patient clinic. ‘Gate-keeping’ became less of a problem as the trial progressed and I believe this was a direct result of the positive feedback that patients and informal caregivers provided. Importantly, the H2H CNS felt that not all attendees at the CC were grateful for the intervention. In particular, there were instances that members of the community palliative care team did not engage at the CC. It is possible that this is because they felt that the H2H CNS was trying to give them advice about an area that they already felt capable of managing. It is not clear whether this may have been related to the evidence based guidelines component of the intervention. This was not reflected in the qualitative interview with the community palliative care nurse. However, this would need to be further investigated in qualitative work for a phase III study.

Most recent models for provision of palliative care encourage a gradual shift, with palliative care provided alongside active treatment from diagnosis of a life limiting illness.(229) Interestingly, very few patients (10%) involved in the study were known to palliative care services prior to referral. As a result, the shift to palliative care (facilitated by the study) was a sudden rather than gradual process. This is likely to have affected the feasibility of the intervention. There were very few negative comments related to the intervention and these related to other relatives (not the informal caregiver) not realising that palliative care would be involved in the intervention and that an end of life discussion would occur as part of the intervention.

Very few GPs attended CCs (less than a third in the FT and less than 50% in the WL group) and in some instances community palliative care refused referrals. It is only after follow up

phone calls and discussions that I would have with the Consultants in the community palliative care team, that the referral would be accepted. This is very different to the cancer H2H model of care being delivered at the Royal Marsden. In the cancer H2H model, there is often 4-5 HPs present at each CC (including GPs) and community palliative care referrals are always accepted. This is likely to reflect the lack of understanding amongst community HPs of the terminal nature of PIF-ILD and their substantial palliative care needs. In the Abernethy CCs, all CCs included the GP, patients and/or family member.(80) In addition, a palliative care representative were present at every CC. The number of participants at the CCs ranged from 5-8. Again these were conducted in the cancer setting where HPs are more likely to have an understanding of the palliative care needs and poor prognosis that patients have. The length of CCs in the Abernethy trial ranged from 20-58mins with a median time of 36mins.(80) In the H2H trial, the median for both the WL and FT CCs collectively was 90 mins with a range of 60-150 mins. Reasons for the longer CCs in the H2H trial are unclear but may reflect trying to manage patients and informal caregivers with very little information about the terminal nature of their disease or HPs' uncertainties and lack of confidence around management.

At the CC, patients and informal caregivers as well as the HPs were given the evidence based guidelines. Patients, informal caregivers and HPs indicated that they were grateful for the guidelines as they allowed systematic delivery of symptom control and provided reassurance that they were already "doing the right thing".

5.6.3 **Aim 3-To inform methods for a future randomised controlled trial**

Despite many of the points raised by Shanyinde et al (212) that were successfully achieved in this trial, not all the criteria set pre-study were met. Even though both the consent rate and recruitment numbers were realised, only 24% of the FT group received the CC within the 14 day allotted timeframe that is well below the 80% feasibility criteria. This was largely due to the difficulty in getting HPs to schedule a CC within one week's notice. Interestingly, Abernethy et al (80) also observed it was difficult to ensure that CCs were held within 28 days with only 38/167 CCs being held within this time period. They noted that CCs often became more of a priority to organise when there were changes in clinical status. Certainly in qualitative work done by Mitchell et al (76) following their RCT, both GPs and palliative care teams felt that routine CCs

were less useful than those held at critical points in the patients' illness (before discharge home or when there were complex issues). Abernethy et al (80) suggest that it may be necessary to align timing of CCs with clinically determined need. In any future trial, if the Fast-track design was used, the time between randomisation and CC for the FT group and subsequently the time before the WL group receive the intervention would need to be increased to ensure that there was enough time for the H2H CNS to organise the CC for the FT group.

Interestingly, there appeared to be a greater change in outcomes in the WL group between week 4 and week 8 than the FT group between baseline and week 4. This may be related to the fact that the majority of the CCs for the FT group could not be organised within the 2 week time period but the majority of the WL CCs were organised within their 2 week allocated period. This may have resulted in a more marked difference between the week 4 and week 8 WL data compared to the baseline and week 4 data of the FT group and the full effect of the intervention may have been under estimated at the primary end point of 4 weeks. However, Mitchell et al (78) CC group showed better maintenance of physical and mental health measures of QoI in the 35 days before death. It was suggested that CCs may improve clinical relationships and care plans at referral, which were not implemented until severe symptoms develop or the patient becomes less well. The authors hypothesise that this is because of improved links between GP and specialist teams, and the development of more effective care plans that are enacted when the rapid deterioration experienced in the terminal phase takes place. It is not clear from this trial if this is the case and compliance of participants with the intervention, more information surrounding quality assurance post CC and further formal outcome measures post CC would be needed before this could be ascertained.

The trial opened to recruitment 10/2011 and research CNS cover was in place to allow recruitment during my maternity leave 11/2011-6/2012. However, only 1 patient was recruited during this time. On reflection this is because a medical presence was required in the ILD clinics to identify potential patients and to discuss and challenge ILD doctors about their management and potential benefit for patients. This is especially important in a speciality in which there has historically been poor palliative care involvement.

The H2H intervention is a complex intervention with multiple different active components. As a result, there will inevitably have been some variation in the manner in which the service

received by individual patients and informal caregivers. Implementation fidelity is “the degree to which...programs are implemented....as intended by the program developers”. (230) Only by understanding and accurately recording how a complex intervention has been delivered, can a more detailed understanding of how and why the intervention works be achieved.(231) For instance, a study of a parent training programme found that when the programme was implemented with high fidelity, the parenting practices improved significantly, but the effect was much less when implementation fidelity was low.(232) As discussed, attempts were made to standardise delivery of the intervention as much as possible with training, observation of delivery of the CC, proformas and evidence based guidelines. This level of standardisation does seem reasonable considering the time and cost restraints. However, if the H2H service were to be further evaluated in an **Evaluation** trial, it would be important to ensure further standardisation of the service delivered by including a measure to determine the consistency with which the intervention was delivered. The CCs could be audio or video taped to give feedback of performance to the H2H CNS with subsequent training to promote consistency. In addition, this would allow detailed information to be gathered on the content of the CC which may provide insight on the mechanisms of effect of the complex intervention and allowed deeper consideration and understanding of which part of the complex intervention is effective. In hindsight, it would have been useful if compliance of patients and informal caregivers had also been recorded. This may have provided valuable information on how outcomes for users may differ between compliant/non-compliant patients and informal caregivers. Recording this information is unlikely to have been too burdensome in terms of cost or time and would have been helpful in considering the real life implications of delivering this service within the NHS.

Future work needs to consider which specific aspects or components of the H2H intervention are effective. For example, it is difficult to know whether the benefit from the intervention is due to the CC or palliative care involvement. Certainly patients who receive timely palliative care will have better co-ordination of services, symptom care, emotional support, education and family support and this is something that the H2H intervention facilitates. In developing understanding into the active ingredients in the H2H intervention, the CC needs to be examined more closely during delivery. Aspects which need to be considered include content of each CC, themes considered and the interaction with patients, carers and HPs. This may be done through quantitative or qualitative measures. This may provide valuable information on how the H2H

intervention is working in the PIF-ILD setting and how and why this differs to the cancer setting or to normal specialist palliative care input. In the Abernethy et al RCT, there were positive effects of both the CCs and patient/caregiver educational visits (80) therefore future studies should include an attention control to determine whether the intervention *per se*, ie the added face-to face time with care providers, or a combination of both accounted for the change in outcomes. In addition, future work should consider how implementation of the H2H intervention fits within conceptual theoretical models such as Normalization Process Model (233) prior to embarking on a phase III study. This may allow a better understanding of how to normalise the H2H intervention within ILD clinical practice.(234)

In the Mitchell et al study (78), the CC was conducted between specialist palliative care teams and GPs via telephone. The study was conducted in the cancer group and patients and informal caregivers were not involved in the CCs. Telephone participation for GPs (rather than face-to-face participation) was felt to be a less successful form of communication when used in a RCT looking at case conferencing in Australia.(235) It is difficult to know whether this form of mode of delivery could be used in this group effectively but warrants further investigation.

The RCT was carried out at a specialist centre in London therefore generalisability nationally and internationally may be limited; this warrants further investigation. In addition, the majority of the patients were White British. It may be argued that the palliative care needs for these patients may vary across different cultures. However, the qualitative work in the **Development** stage was conducted across KCH and RBH. KCH has a very different socio-demographic patient group to RBH. Importantly, this showed no difference in the palliative care needs of the patients and informal caregivers interviewed across the 2 hospitals. Within the constraints of cost, it was not possible to make the RCT multi-centre. However, any future **Evaluation** trial would ideally need to be multi-centred, national and if possible, international to assess outcomes across different cultures and to ensure generalisability of findings.

The RCT was a phase II trial and was therefore not powered to show efficacy. Any positive results should be interpreted with caution and need to be evaluated in an adequately powered trial.

Delay in delivering the FT CCs affected comparison of the efficacy of the intervention at the primary endpoint of 4 weeks. However, this is likely to have under-estimated rather than over-

estimated any effect. In addition, referrals to community services for WL group were made at randomisation and a few community services contacted (and sometimes visited) with the patients and informal caregivers (exact numbers unknown and not recorded) before the CC. This may also have potentially diluted the effect size of the intervention. In hindsight, it would have been preferable to not make any referrals to community services for the WL group until after 4 weeks. However, it is only when these referrals were made, that a date for the CC could be set. Consideration needs to be given between achieving a balance of allowing enough notice to community HPs to set a convenient date for the CC and not contaminating the WL group with contact from community HPs prior to the CC. On reflection, it would also be useful to have noted how many community HPs had made contact and the nature of the contact.

At follow up, the H2H nurse contacted the patient/informal caregiver 2 weeks, 4 weeks and 2 months after the CC. This involved the H2H CNS discussing with the patient or informal caregiver whether outcomes from the care plan had been achieved. It would have also been beneficial to have assessed with more uniformity (e.g. a needs assessment tool) at the CC, the 2 week, 4 week and 2 month follow up, what baseline and subsequent needs there were for the patients and informal caregivers. This would have provided helpful information on whether the intervention was meeting unmet need identified at the CC. This is unlikely to have added to time or cost.

A potential outcome measure which could be used is the Leicester Cough Questionnaire which has been validated in ILD. As discussed previously, informal caregivers may be an influencing factor on symptom control measures. Therefore, in any future RCT, patients ought to be stratified on whether they have informal caregivers or not. In addition, there would need to be strict control of referrals to community HPs to ensure that the WL group are not referred and subsequently receiving community support prior to the CC. This may be facilitated by not passing the details of the patients to the H2H CNS before the WL period has expired.

To improve return of questionnaires after receiving the CC- It is possible that if a research nurse were to arrange to complete the questionnaires in person with the patient and informal caregiver, this may improve attrition post the CC.

5.6.4 **Limitations**

The trial took place in a specialist ILD unit in central London and therefore its generalisability is likely to be restricted. This was a phase II trial and was therefore not powered to show efficacy. Any positive results should be interpreted with caution and need to be evaluated in an adequately powered Evaluation trial. In addition the difficulty in being able to conduct the FT CCs within one week of randomisation resulted in some difficulty in being able to compare the efficacy of the intervention at the primary endpoint of 4 weeks. However, this is likely to have under-estimated rather than over-estimated any effect.

The H2H intervention is a complex intervention with multiple different components. Attempts were made to standardise delivery of the intervention as much as possible with proformas and evidence based guidelines. However, there will have been some inevitable variation in the intervention delivered between each CC. In addition, there was a changeover of H2H CNS during the study which will have introduced some variability to the delivery of the intervention. To limit this, both H2H CNSs underwent the same training in delivering the intervention which included quality assurance observation which helped to keep this bias to a minimum.

The participants for the qualitative interviews were chosen by the H2H CNS. It is possible that she may have chosen only those patients, informal caregivers and HPs who had had a positive experience influencing the outcome at interview and this may have introduced some bias. I conducted the majority of the qualitative interviews. The patients and informal caregivers were already aware of my role within the research team. This may have influenced the qualitative interviews and made patients and informal caregivers less likely to make negative comments about the intervention.

5.6.5 **Implications for clinical practice**

Resistance to accepting referrals to CPCT is likely to reflect the bias in England's CPCT to malignant work and a lack of understanding of the palliative care needs of PIF-ILD patients (supported by preliminary qualitative work). This is clearly an area for education and development going forward.

The qualitative work from this trial also found that some patients had not been referred earlier in their disease journey to palliative care by community HPs. This was despite requests from patients and informal caregivers. There was also some gatekeeping by hospital HPs who felt that some patients were not “*ready to hear they were palliative*”. This was also mirrored in the refusal of some patients to take part in a “*palliative care trial*”. It is clear that there is still a misconception that palliative care is a last resort and referral should only be made at the end of life. This is despite the World Health Organisation’s advice (20) that palliative care should be delivered in parallel to active care once a life-limiting illness has been recognised. Supporting this, recommendations of both the British Thoracic Society (12) and NICE (236) state that palliative care teams should be involved in patient management to ensure adequate symptom control and psychological support. If palliative care is only delivered at the end of life, patients and informal caregivers may be denied valuable symptom control and psychosocial support in earlier stages of the disease and important decisions around end of life preferences may not be explored. Strategies on improving the knowledge of patients, informal caregivers and HPs on the benefits of early palliative care need to be explored.

The background qualitative work identified that HPs did not feel confident in managing the symptoms of patients with PIF-ILD. During the H2H CC, the evidence based symptom control guidelines were discussed and distributed with targeted education of HPs as needed. This highlighted that HPs required support regarding symptom control in this non-malignant group. Strategies to improve HPs’ knowledge in managing the symptoms of patients with PIF-ILD are needed to improve the future care of these patients. In addition, patients and informal caregivers at the beginning of the study expressed a lack of confidence in community HPs’ ability to manage PIF-ILD- strategies to improve this relationship are needed. Abernethy et al (80) suggested that the CC may be used to identify gaps in knowledge and provide targeted teaching to community HPs. This was done in an informal way through the H2H CC through the use of the evidence based guidelines. However, in the future, identification of educational needs could be recorded in a more uniform way with formal evaluation in changes in knowledge.

5.7 Conclusion

The aims of this mixed methods trial looking at the H2H intervention in PIF-ILD patients were to begin to evaluate H2H in a phase II study, to evaluate the H2H intervention in terms of feasibility and acceptability in a phase II study and to inform a future larger RCT (RCT phase III/**Evaluation** trial). Preliminary evidence from this trial suggests that there may be a positive effect on both patients and informal caregivers of the H2H intervention on palliative care needs, QoL and anxiety and depression. In addition, the intervention may manage uncertainty by facilitating early discussion about disease progression, improving communication and addressing end of life planning needs. There may also be effects on death rates and survival related to early use of a palliative care intervention which warrant further investigation. The H2H intervention appears to be both largely feasible and acceptable.

As this is a phase II study, any positive effects may be promising but would need to be further examined in a full-scale phase III study forming part of the **Evaluation** phase of the MRC guidance before conclusions about effectiveness may be drawn. Despite this, the information obtained from this trial will allow sample size calculation in future studies, has provided valuable information on the spectrum of needs of patients and informal caregivers affected by PIF-ILD, the potential effects of the H2H intervention and the feasibility and acceptability of delivering the H2H intervention in this group. As this study is underpowered, negative or borderline results of outcomes should not prevent further development and investigation of the effects.

Chapter 6 Summary and Discussion

6.1 Summary

The aim of this thesis was to develop and evaluate a complex intervention, which comprised a new service, in PIF-ILD by adopting the MRC complex intervention guidance supported by the MOREcare guidance as the methodological approach. The adapted service was developed after qualitative interviews. This formed the **Development** stage of the MRC guidance. The adapted service was then tested in a RCT in the **Feasibility/Piloting** stage of the MRC guidance. The RCT found that there were improvements in patient QoL, anxiety and depression scores and informal caregiver anxiety and depression scores. The adapted service and study design were largely both feasible and acceptable.

6.2 Discussion

6.2.1 Summary of objectives

To develop the service and then evaluate it, I needed to complete 8 sequential objectives. Each of these objectives and the findings from this study will be briefly summarised here and the findings from this research compared and contrasted to previous research in PIF-ILD or other relevant areas.

The findings from objectives 1-3 formed the *identifying theory/developing theory and modelling theory/processes* stage of the **Development** stage of the MRC guidance:

The first objective was to identify and describe the specialist palliative care needs within the PIF-ILD population. Qualitative research interviewed patients and for the first time, informal caregivers and HPs. Many patient participants reported that the main physical symptoms associated with PIF-ILD were dyspnoea and cough. This supports what has been found previously in two qualitative studies conducted in the Netherlands and USA (37, 38) and that found by Schoenheit et al (36) in their in-depth interviews with 45 IPF patients from five European countries. The findings from the qualitative work in the **Development** stage agreed

with the Swigris et al (38) and Schoenheit et al (36) studies which found that dyspnoea and cough were found to be distressing, sleep quality was affected and low energy or exhaustion affected daily activities. The findings from this qualitative work also found similarities to other disease groups' experiences. Dyspnoea as a reminder of one's mortality has been seen in COPD patients, disability with social isolation and depression has been seen in heart failure patients and anxiety/panic associated with bad episodes is similar to that previously seen in MND patients.(237) Furthermore, similar to that found by Swigris et al (38), patients were worried about being a physical burden and PIF-ILD led to decreased ability to undertake sexual activity. Interestingly, participants in this study did not appear to have financial concerns nor did they worry about paying for medical care which were found by both Swigris et al (38) and Schoenheit et al (36). This is likely to reflect that the majority of patients were of retirement age and that patients in the UK do not pay for NHS medical care.

The qualitative research conducted as part of this study adds to the previous data by revealing that the burden of these palliative care needs is more considerable than previously noted with impact on every aspect of patients' and informal caregivers' lives with the psychological impact greater than previously noted. This research showed a more pronounced strain than previously noted in spousal relationships. This may be because through interviewing informal caregivers, the full impact of the disease on relationships and the family unit as a whole is revealed. Informal caregivers provide valuable support to patients and often enable them to stay in their preferred place of care. Whilst support for informal caregivers has been addressed in part in the cancer population towards the end-of-life (238, 239), there is no current literature for the ILD population and this should be a priority for further research. Interestingly, some of the HPs had limited appreciation of the palliative care needs of patients and the psychosocial effects on both patients and informal caregivers. In addition, there seemed to be resignation amongst some HPs that patients would inevitably suffer poor symptom control. This appeared to be partly due to some HPs' lack of knowledge and misconceptions of effective symptom control interventions. This is the first time that HPs' views on the palliative care needs of those affected by PIF-ILD have been researched and therefore there are no previous studies to compare to. However, it is important that HPs understand informal caregiver experiences of PIF-ILD and what support they require in caring for someone with PIF-ILD. In addition, the disparity in the knowledge of how to manage symptoms is important. Education of symptom control interventions may empower

HPs to deliver effective specialist palliative care to these patients where they have not previously felt confident to do so.

The second objective was to identify patients', informal caregivers' and HPs' perceptions on co-ordination of care, communication and information needs. The qualitative research conducted in this study for the **Development** phase (same study sample as Objective 1) showed a good general understanding from both patients and informal caregivers that PIF-ILD is a serious illness which is terminal. This finding supports what has previously been noted: Quantitative analysis of the perceptions of illness in IPF patients and their family members in one previous study is limited as numbers were small (N=32). However it observed that most patients understood their disease to be a 'serious condition' and that family members understood the patient might not survive (N=16).(39) Interestingly, in the qualitative interviews for the **Development** phase, this realisation appeared to be a gradual process and often precipitated by deterioration in health rather than any formal information provided. There is no previous literature on end of life planning and decision making in PIF-ILD. Importantly, no patients had made end of life plans. In addition, informal caregivers had not had conversations concerning end of life decisions such as preferred place of care and preferred place of death with their loved ones. This supports similar findings in other non-malignant diseases such as heart failure.(44) Challenges were apparent. First, some informal caregivers did not know how to broach the subject. Second, patients had unrealistic perceptions of how their disease would progress and how the terminal stages would manifest. This led to unrealistic perceptions that they would not need care or help at the end of life. However, the willingness of participants to discuss their preferences was clear. Clinicians caring for patients with PIF-ILD face a challenging task regarding information needs for both patients and informal caregivers. They are a group of conditions that the general public is on the whole unfamiliar with and so natural introductions to questions regarding prognosis and end of life care are usually not initiated by patients themselves. In contrast to malignant disease, this places the onus for developing such conversations almost completely with the HP, in the main a respiratory physician. In the context of busy clinic appointments during which information regarding diagnosis, treatment options and medical care also has to be communicated it is not surprising that the uncomfortable topic of end of life care is neglected. However, the qualitative work in this study shows the importance that patients and their informal caregivers place on these issues.

Previous studies have identified that patients are often prescribed sub-therapeutic doses of information; a recent quantitative survey of 52 defined choice and open-ended questions of 1448 IPF patients and informal caregivers conducted in the United States reported that two-thirds of respondents felt there was a clear lack of information.(40) Also, Schoenheit et al (36) found in their qualitative study of 45 European IPF patients that there was a lack of information provided to them about their disease. In the cancer setting, clinicians tend to underestimate the amount of information that patients require.(240, 241) In fact, a large multi-centre UK cancer study (2331 patients) showed that 87% of participants wanted to know all information, both good and bad news.(242) This is the first qualitative research which has been done in PIF-ILD which has also examined informal caregivers' information needs. This research has shown that patients and informal caregivers felt that information provided about the future was lacking and could be improved. All HPs recognised the importance of providing information about prognosis and end of life with accurate prognostication and timely conversations to ensure that patients and informal caregivers had the opportunity to make end of life plans. Despite this, many informal caregivers reported receiving information from other sources for example the internet; the delivery of difficult news that the disease was terminal was not from the doctor. Patients and informal caregivers felt it was the HPs' responsibility to provide them with information and to be able to judge what information should be provided when. Both patients and informal caregivers expressed a wish to receive more information from clinicians and implicitly trusted ILD HPs to deliver this information at the most appropriate time. HPs recognised the difficulty of balancing information needs with maintaining hope and often struggled with conducting discussions around end of life issues. However, HPs did not feel that this was done well. In addition, many patients in the cancer setting assume that the doctor would have told them everything relevant.(243) This was similar in this study where patients were trusting in the skills of doctors. Literature repeatedly states that patients have high information needs and wish to be kept well informed about their illness regardless of diagnosis.(244, 245) However, whilst the physical care skills of respiratory clinicians may well be excellent, this is not necessarily the case as far as effective communication of end of life issues are concerned.(246) It may be the case that there is a purposeful non-disclosure of information which may result from poor training or a lack of awareness of the impact that a failure to disclose has on patients and informal caregivers.(246) This qualitative research showed that patients and informal caregivers wanted to know but might be too afraid to ask. This is similar to what has been seen in other non-malignant disease

groups. (45) Clinicians need to anticipate this and continuously assess patients and informal caregivers' information needs throughout the disease trajectory and although discussions about prognosis in time pressured clinics are difficult, HPs can learn effective communication skills to assist them in delivering this information sensitively.(247-249) This is especially important as research conducted in other non-malignant disease groups has identified that limited discussion between patients, informal caregivers and HPs directly addressing patients' and informal caregivers' concerns has been shown to affect psychological morbidity.(44)

It has been noted that there is inadequate communication between HPs.(250) This study also found that there was poor communication between the acute and primary care setting leading to frustration for patients, informal caregivers and HPs alike. There was also a feeling that malignant diseases had much better communication surrounding end of life issues than was currently being seen for PIF-ILD patients. It is not clear whether this is due to non-recognition of the terminal phase or inadequate provision for communication. In addition, this qualitative work found that there was poor co-ordination of care with reliance on the specialist ILD centre and a lack of confidence in community services. Schoenheit et al (36) found in their study of 45 European IPF patients interviewed, that the majority of participants had experienced delayed diagnoses and criticised the care they received, while a minority of participants who were diagnosed promptly reported their care more positively. The results from the qualitative work in this study supported the need for the development of a palliative intervention for this group of patients which aimed to improve communication and co-ordination of care whilst facilitating discussions surrounding information needs and important end of life preferences.

The third objective was to identify patients', informal caregivers' and HPs' views on the H2H model of care and ways in which it may be improved/adapted for the PIF-ILD population. The qualitative work showed that the vast majority of patient, informal caregiver and HP participants felt that the model of the H2H intervention was an excellent one and were overwhelmingly supportive of it. Patients and informal caregivers valued knowing a plan of action of who to contact in a crisis as they felt that this was lacking. In addition, HP participants felt that clearly allocated roles and responsibilities which were communicated across the board would be helpful in ensuring that all HPs took appropriate responsibility when necessary. Community HPs felt that the CC model of care would facilitate them to take a more prominent role in the end of life care of patients whilst being supported by the specialist ILD centre. Very few concerns were

made about the model of care but one included the difficulty of being able to get all HPs to attend a CC at the same time.

The findings from objective 1-3 were integrated with the background work to present the adapted H2H model of care as objective 4.

Objective 5 focussed on defining appropriate outcomes and measures for the adapted H2H intervention. Appropriate outcomes and measures for the adapted H2H intervention were chosen through information provided by the background systematic review and qualitative work forming the *modelling theory/processes* phase of the **Development** stage. The systematic review identified that there were a wide range of symptom control and QoL outcome measures that had previously been used in interventional studies (23 and 6 different outcome measures for symptom control and QoL respectively). In addition, there were no validated outcome measures used in interventional studies. In choosing outcome measures for the H2H trial, to aid comparison, some outcome measures that had previously been used in the H2H cancer study at the Royal Marsden Hospital were used. The primary outcome measure chosen for the **Feasibility/piloting** stage was the POS. This appeared to be an appropriate outcome measure as the qualitative work forming part of the **Development** phase identified that patients had holistic palliative care needs which did not just focus on symptom control or QoL but encompassed every part of the patient's life.

Objectives 6-8 formed the **Feasibility/Piloting** stage of the MRC guidance:

Objective 6 focussed on beginning to evaluate the adapted H2H service in a phase II study. The FT RCT conducted provided preliminary information related to the outcomes chosen in objective 5. The quantitative results showed a positive and significant effect on patients' POS scores at the primary endpoint of 4 weeks with a mean change score of 5.7 points in the FT group which was sustained at 8 weeks. In addition, there was improvement in the WL POS score between week 4 and week 8 of 4.3 points. For the POS, a variation of one point in individual items is linked to clinical meaningful change.(161) This suggests that the H2H intervention may improve the palliative care needs of PIF-ILD patients in a clinically meaningful way. The 2 RCTs that have previously trialled CCs in the cancer setting (78, 80) have not used the POS or a global palliative care assessment tool so a direct comparison cannot be made on effectiveness in the PIF-ILD setting.

At the CC the evidence based guidelines were used and a comprehensive palliative care assessment (including symptom control, psychological, social needs and crisis management plan) was carried out. Ongoing management of the patients' palliative care needs were carried out by the community teams. It is possible that the intervention of the evidence based guidelines and the ongoing management of the palliative care needs identified at the CC, resulted in the improvements in the patients' POS seen. It is difficult to know whether the benefit from the intervention seen is due to the CC, palliative care involvement or the added time with care providers. However, the results are promising and warrant further investigation.

Of note, the WL group had a higher percentage of informal caregivers. Informal caregivers play a vital role in the management of symptoms in the home setting.(217) In addition, HPs providing palliative care in the community setting report that they rely on informal caregivers' assessments of the patients' condition and use them as cues for action.(217) Therefore it may be expected that if a patient does not have an informal caregiver, this interface is more difficult potentially leading to more unmet palliative care needs. The WL group also had a higher GP, DN and CPCT presence at the CC than the FT group. This may have influenced outcomes as it would be the GP, district nurses and CPCT who would instigate the symptom control interventions and manage the patients' palliative care needs on a day to day basis. However, this may have led to

false improvements in the WL scores which would only have diluted the effect size, suggesting that the potential effect of the intervention may be greater than reflected in the scores.

There was also an improvement in QoL scores on both the KBILD and SGRQ impact and total scores at week 4 in the FT group. The improvement in the WL SGRQ impact and total scores were marked between week 4 and week 8 where both domains showed improvement greater than the Minimal Important Clinical Difference (MID) for IPF. Mitchell et al (78) investigated the impact of a telephone CC between GPs and specialist palliative care teams (without the patient or informal caregiver present) in a RCT of 159 cancer patients in Australia. They found that the primary outcome- global QoL was not influenced by the intervention but the CC group showed better maintenance of physical and mental health measures of QoL in the 35 days before death. The authors suggest this is because care plans at referral were not implemented until severe symptoms developed. Though the Mitchell et al study was a CC to meet professional needs, whilst the H2H service was a patient-centred, face-to-face intervention involving, patients, informal caregivers and HPs. This may have been an influencing factor. The QoL measures used in the Mitchell et al study were the Assessment of Quality of Life at the end of Life (AQEL) (219), the McGill Quality of Life Questionnaire (220) and the Subjective Wellbeing Scale (221) so direct comparisons between the two studies are not possible. Interestingly, the complex intervention of a breathlessness intervention service delivered by Higginson et al study (222) also showed some improvements in QoL domains. The Higginson et al study is a RCT of 105 patients with refractory breathlessness which included ILD patients. It found that the patients who received the integrated palliative care and respiratory breathlessness support service had, at 6 weeks, significantly improved breathlessness mastery, a domain of the Chronic Respiratory Disease Questionnaire. Mastery assessed patients' feeling of control over their breathlessness and its effects on QoL and function, and was on average 16% higher for those patients receiving the breathlessness support service. However, numbers of ILD patients were small 19 (18%) and ILD patients' diagnoses were not differentiated.

There were improvements in anxiety and depression of both patients and informal caregivers at week 4 in the FT group. This effect appeared to be sustained in the FT group with continued improvement in scores at week 8. In addition, there was marked improvement from week 4 to

week 8 in the WL group which was greater than the MID for COPD on the HADs. Even though the HADs has not been validated in IPF, the MID for COPD has been used previously for IPF patients.(223) Lindell et al (113) conducted a mixed methods RCT of 21 patients looking at a disease management program delivered using a format of support group for both IPF patients and informal caregivers with a control group of best usual care. In contrast to this trial, they found that on quantitative analysis, there was increased anxiety and decreased QoL in the intervention group. However, the qualitative work showed that patients did not feel isolated and felt the intervention had enabled them to put the disease into perspective, gave comfort and provided an improved mental picture. The quantitative and qualitative work in this trial is in agreement. The qualitative work in the H2H trial showed that the community palliative care teams were providing similar support to patients and informal caregivers. In the Higginson et al study(222) of their breathlessness intervention service, there were also non-significant improvements in depression. In the H2H trial, the effect on anxiety and depression scores was also mirrored in the informal caregiver results with improvements in the depression and total HADs scores at week 4 in the FT group and much larger improvements (greater than the MID) in the WL group between week 4 and week 8 in all 3 domains of the HADs. These improvements in anxiety and depression scores in both the patient and informal caregiver were supported by the qualitative results.

There were also large improvements in the ZBI and CQLC between week 4 and week 8 in the WL group. In the Mitchell et al study(78), there was a positive impact on caregiver burden with significantly lower carer burden in two of the five domains (impact on schedule and lack of family support) on the Caregiver Reaction Assessment (79) as well as the total score. Knowing what to monitor, how to interpret the signs successfully and when to inform a HP were all issues of concern for informal caregivers in a previous palliative care study.(217) In the H2H trial, a copy of the individualised care plan made at the CC was given to the patient, informal caregiver and HPs involved in the care of the patient. This included direct contact numbers for all HPs and step-wise instructions of what to do in the event of deterioration. Patients, informal caregivers and HPs expressed in the qualitative interviews that they were very grateful for this individualised care plan with patients and informal caregivers expressing that this greatly reduced their anxiety and HPs expressing that it allowed them to provide better care. In addition, the qualitative data suggests that the intervention facilitated improvement in both the

co-ordination and efficiency of care delivered with patients and informal caregivers expressing that they now felt that they were “*Fast-tracked*” through the system as HPs had been made aware of the seriousness of their condition. Qualitative results suggest that this resulted in patients and informal caregivers being able to access help when needed. The actual process of the CC, having a clear individualised care plan and being supported in this way by the community HPs may have helped to reduce both patients’ and informal caregivers’ anxieties seen in the quantitative results.

The H2H intervention aimed to manage uncertainty by facilitating early discussion about disease progression, improving communication and addressing end of life planning needs. At the CC, not all patients wanted to talk about advance care planning decisions such as PPC and PPD. This was also found in the cluster randomised study conducted by Abernethy et al (80) where prognosis, end of life issues and previous experiences of death and dying were rarely discussed at the CC for cancer patients. For those patients who did discuss advance care planning at the H2H CC, even though it could initially be distressing for relatives present, it was seen as incredibly useful. For some patients, the CC gave permission to conduct these important conversations. However, many patients who had not wanted to discuss these issues at the CC, then went on to have subsequent discussions with their community HPs in the weeks after the CC. It is possible that planting the seed of thought about these important issues at the CC precipitated these conversations and decisions. This is in itself an important influence that the intervention may have had.

Objective 7 was to evaluate the H2H intervention in terms of feasibility and acceptability. There were no set criteria for feasibility or acceptability which had previously been used for complex interventions within the MRC guidance. Therefore after reviewing previous studies, feasibility criteria of: consent rate of >25%, recruitment of 52 patients and 80% of patients in the FT group were able to receive the H2H intervention within 14 days of their allotted time were set. Even though both the consent rate and recruitment numbers were met, only 24% of the FT group received the CC within the 14 day allotted timeframe. This was largely due to the difficulty in getting HPs to be able to schedule a CC within one week’s notice. This in turn led to some difficulty when conducting analyses at the 4 week point and may have led to under-estimation of

the effect of the H2H intervention. Abernethy et al (80) also find it difficult to ensure that CCs were held within 28 days with only 38/167 of their CCs being held within this time period. The study design of a FT randomised controlled trial however worked well and is likely to be an influencing factor as to why recruitment rates were met.

Qualitative work conducted during the RCT showed views of the H2H intervention as expressed by patients, informal caregivers and HPs to be extremely positive and the intervention was acceptable. Support in the community for patients and informal caregivers before the start of the study was minimal. All patients and informal caregivers interviewed were very grateful to have received the H2H intervention. Patients, informal caregivers and HPs alike praised the CC model of care. In previous qualitative work following the Mitchell et al RCT, GPs reported that the CC allowed them to be better informed, made discharge planning easier and allowed clear delineation of role between the GP and the palliative care service.(76) All of these findings were supported in this trial. Very few GPs attended CCs (less than a third in the FT and less than 50% in the WL group) and in some instances community palliative care initially refused referral for these patients. In the Abernethy et al study (80), all CCs included the GP, patients and/or family member and a palliative care representative. The poor attendance of community HPs in the H2H trial is likely to reflect the lack of understanding amongst community HPs of the terminal nature of these diseases and their substantial palliative care needs.

Objective 8 was to use the Phase II study to inform a future larger randomised controlled trial (RCT phase III/**Evaluation** study). The Phase II study has provided valuable information on appropriate time periods between randomisation and CC. There is clearly a need for a greater time period between randomisation and the CC in the FT group if this trial design were to be used again. In addition the Phase II study has highlighted that mechanisms need to be put in place to minimise attrition after the CC has been delivered. The information provided from the phase II study has enabled calculation of a sample size for any potential phase III study.

6.2.2 Limitations of thesis

The retrospective review of medical notes used in the *identifying/developing theory* phase of the **Development** stage is limited. As such, palliative care needs identified through this piece of work have been taken treated with caution and this piece of work has been used as background in this study.

For both the qualitative work in the **Development** and **Feasibility/Piloting** stages, numbers were small so information is limited. However, this is the first time a complex intervention looking at improving symptom control or QoL has been developed in this group of patients using the MRC guidance. Therefore information provided as a result of this study is especially important. For the qualitative work conducted as part of the **Development** work, on analysis of the later interviews, no new themes were emerging. Therefore, it is unlikely that further interviews would have made any difference to the conclusions drawn. However, for the qualitative interviews conducted as part of the **Feasibility/Piloting** stage, participants for interviews were identified by the H2H CNS from patients, informal caregivers and HPs who had completed the H2H trial. This is likely to have introduced bias into the sample as she may have identified participants who were more likely to be positive about the H2H intervention. In addition, due to time and cost limitation, a pre-determined set number of interviews (5 patients, 5 informal caregivers and 5 HPs) were conducted. However, there was ongoing emergence of themes in later interviews. It is possible that there were further themes that may have emerged if further interviews had been conducted. This may have affected the qualitative outcomes in the **Feasibility/Piloting** stage. However, as I was also running the RCT, I do not think it would have been realistic for me to have conducted any more interviews. In conducting qualitative work in future trials for H2H, I would approach all participants who received the H2H intervention sequentially to limit bias and interview patients, informal caregivers and HPs until there was saturation of themes.

The H2H intervention is a complex intervention with multiple different active components. As a result, there will have been some variation in the service received by each patient and informal caregiver. As discussed in Chapter 5, attempts were made to standardise delivery of the intervention as much as possible with training, observation of delivery of the CC, proformas and evidence based guidelines. This level of standardisation does seem reasonable considering the time and cost restraints. However, if the H2H service were to be further evaluated in an

Evaluation trial, it would be important to ensure further standardisation of the service delivered by including a measure to determine the consistency with which the intervention was delivered. The CCs could be audio or video taped to give feedback of performance to the H2H CNS with subsequent training to promote consistency. In addition, this would allow detailed information to be gathered on the content of the CC which may provide insight on the mechanisms of effect of the complex intervention and allowed deeper consideration and understanding of which part of the complex intervention is effective. In hindsight, it would have been useful if compliance of patients and informal caregivers had also been recorded. This may have provided valuable information on how outcomes for users may differ between compliant/non-compliant patients and informal caregivers. Recording this information is unlikely to have been too burdensome in terms of cost or time and would have been helpful in considering the real life implications of delivering this service within the NHS.

The RCT was carried out at a specialist centre in London therefore generalisability nationally and internationally may be limited and warrants further investigation. In addition, the majority of the patients were White British. It may be argued that the palliative care needs for these patients may vary across different cultures. However, the qualitative work in the **Development** stage was conducted across KCH and RBH. KCH has a very different socio-demographic patient group to RBH. Importantly, this showed no difference in the palliative care needs of the patients and informal caregivers interviewed across the 2 hospitals. Within the constraints of cost, it was not possible to make the RCT multi-centre. However, any future **Evaluation** trial would ideally need to be multi-centred, national and if possible, international to assess outcomes across different cultures and to ensure generalisability of findings.

The RCT was a phase II trial and was therefore not powered to show efficacy. Any positive results should be interpreted with caution and need to be evaluated in an adequately powered trial.

Delay in delivering the FT CCs affected comparison of the efficacy of the intervention at the primary endpoint of 4 weeks. However, this is likely to have under-estimated rather than over-estimated any effect. In addition, referrals to community services for WL group were made at randomisation and a few community services contacted (and sometimes visited) with the patients and informal caregivers (exact numbers unknown and not recorded) before the CC.

This may also have potentially diluted the effect size of the intervention. In hindsight, it would have been preferable to not make any referrals to community services for the WL group until after 4 weeks. However, it is only when these referrals were made, that a date for the CC could be set. Consideration needs to be given between achieving a balance of allowing enough notice to community HPs to set a convenient date for the CC and not contaminating the WL group with contact from community HPs prior to the CC. On reflection, it would also be useful to have noted how many community HPs had made contact and the nature of the contact.

At follow up, the H2H nurse contacted the patient/informal caregiver 2 weeks, 4 weeks and 2 months after the CC. This involved the H2H CNS discussing with the patient or informal caregiver whether outcomes from the care plan had been achieved. It would have also been beneficial to have assessed with more uniformity (e.g. a needs assessment tool) at the CC, the 2 week, 4 week and 2 month follow up, what baseline and subsequent needs there were for the patients and informal caregivers. This would have provided helpful information on whether the intervention was meeting unmet need identified at the CC. This is unlikely to have added to time or cost.

The exact nature of the classification of the RCT has been discussed in detail: A Feasibility study can be a small RCT, it need not have a primary outcome and the usual sort of power calculation is not normally undertaken. The sample size should be adequate to estimate the critical parameters (e.g. recruitment rate) to the necessary degree of precision.(251) Arain et al(251) discuss how feasibility studies do not evaluate the outcome of interest as that is left to the main study. Pilot studies are a version of the main study that is run in miniature to test whether the components of the main study can all work together. It is focused on the processes of the main study, for example to ensure recruitment, randomisation, treatment, and follow-up assessments all run smoothly. It will therefore resemble the main study in many respects, including an assessment of the primary outcome and calculation of a sample size.(252) It has been stated that feasibility and pilot studies are usually distinguished from phase II trials in which some sort of evidence for efficacy is sought prior to embarking on a full phase III trial.(252) When this PhD was originally commenced and a protocol drawn up for the RCT, the original MRC framework was used.(28) In this framework, the Phase II trial is described as “exploratory” with aims which may include those shown in Table 6-1 Page 292.

Table 6-1 Table to show aims of a phase II trial as defined by the MRC framework 2000.

Aim	
Testing acceptability and feasibility	Testing the feasibility of delivering the intervention and acceptability to providers and patients
Designing the main trial	The exploratory trial should ideally be randomised to allow assessment of the size of the effect. This will provide information about the sample size for the main trial
Outcomes	Outcomes for the main trial will be piloted during the exploratory phase.

Therefore for the definition, aims and outcomes of the Phase II trial used to test the H2H intervention, the original MRC framework (28) were used. These aims do not fit neatly into the previous definitions of a feasibility or pilot studies and actually span both definitions. The new MRC guidance (13), states that aims for the **Feasibility/Piloting** stage may include testing procedures for their acceptability, estimating likely rates of recruitment and retention of subjects and the calculation of appropriate sample sizes. The aims of the H2H RCT were to define appropriate outcomes and measures for the adapted H2H intervention, to begin to evaluate H2H, to evaluate the intervention in terms of feasibility and acceptability and to inform a future larger randomised controlled trial. These aims span both the old and new MRC guidance. Because the new MRC guidance has clear advantages over the old MRC framework (as discussed in Chapter one), the new guidance was used as the PhD progressed.

6.2.3 Implications for clinical practice

This study has shown that these patients have a high symptom burden with unmet palliative care needs. In addition, these patients are rarely receiving the support of palliative care services. There is an increasing case for properly resourced ILD services to be developed, similar to those provided for patients with lung cancer, in which specialist nurse and early palliative care involvement is easily accessible. This study supports such a model.

The qualitative work from this study found that some patients had been refused referral to palliative care earlier in their disease journey. This was despite requests from patients and informal caregivers. There was also some gatekeeping by hospital HPs who felt that some patients were not “*ready to hear they were palliative*”. This was mirrored in the refusal of some patients to take part in a “*palliative care trial*”. It is clear that there is still a mis-conception that palliative care is a last resort and referral should only be made at the end of life. This is despite the World Health Organisation’s advice (20) that palliative care should be delivered in parallel to active care once a life-limiting illness has been recognised. Supporting this, recommendations of both the British Thoracic Society (12) and NICE (236) state that palliative care teams should be involved in patient management to ensure adequate symptom control and psychological support. Strategies on improving the knowledge of patients, informal caregivers and HPs on the benefits of early palliative care and how to break down these barriers need to be explored.

The research in this study found that these patients and informal caregivers not only have considerable unmet palliative care needs, but that there are inconsistencies in the provision of HP service delivery in the community. This study has further highlighted the needs of the non-malignant respiratory group. It is clear that clinically we need to spend more time ensuring that the needs of non-malignant disease groups are met so that the level of palliative care received is equitable with the high standard that has become the norm in cancer. There is no guidance on who ought to be involved in the delivery of care for PIF-ILD patients in the community and what the role of these individuals ought to be. As a result, these patients and informal caregivers are “falling through the net”. Recently NHS England has recommended the establishment of ILD specialist centres where ILD care is centred around tertiary hospitals to ensure uniformity of the care delivered in the secondary and tertiary setting.(253) However, there also needs to be uniformity of the care delivered in the community with allocated responsibility and accountability so that these patients receive the same standard of care

experienced by other disease groups such as COPD and cancer throughout their disease journey, but very importantly, in the last year of life. The qualitative work in the **Development** phase showed that there was resignation amongst some HPs that patients would inevitably suffer poor symptom control. This was partly due to some HPs' lack of knowledge and misconceptions of effective symptom control interventions. Use of the evidence based guidelines in this study helped with this, but targeted education is needed. Gradually, the profile of the palliative care needs of these patients is being increased. I have recently been appointed to the NICE IPF quality standards committee. Through this I have helped to ensure that the palliative care needs of these patients and informal caregivers remains on the quality standard and a priority at a national level. However, further national and local work is needed.

Interestingly on referral, 8 community palliative care services refused to take on PIF-ILD patients. This was despite clear explanations of the nature of the study and the patients' palliative care needs. This is likely to reflect the bias in England's community palliative care teams to malignant work and a lack of understanding of the palliative care needs of PIF-ILD patients. In addition, very few GPs attended CCs (less than a third in the FT and less than 50% in the WL group). The poor attendance of community HPs is also likely to reflect the lack of understanding amongst community HPs of the terminal nature of these diseases and their substantial palliative care needs. Publications from this study may help in disseminating information. However, there needs to be targeted education of community HPs to improve this.

6.2.4 **Suggestions for future directions of research in this area**

Further research into the best way to support patients and informal caregivers is needed. Clinicians caring for patients with PIF-ILD face a challenging task regarding information needs for both patients and informal caregivers. PIF-ILD are a group of conditions that the general public is on the whole unfamiliar with and so natural introductions to questions regarding prognosis and end of life care are usually not initiated by patients themselves. In contrast to malignant disease, this places the onus for developing such conversations almost completely with the HP, in the main a respiratory physician. In the context of busy clinic appointments during which information regarding diagnosis, treatment options and medical care also has to be communicated, it is not surprising that the uncomfortable topic of end of life care is

neglected. However, this study shows the importance that patients and their informal caregivers place on these issues. Further research is needed into the most appropriate model to discuss end of life issues with these patients and informal caregivers. For example, different ways for expressing life expectancy, facilitating hope and discussing the dying process. Both quantitative and qualitative methods would be helpful and studies of bereaved informal caregivers' experiences in discussing this topic may obtain useful data both from the point of view of the informal caregiver and their perception of the patients' needs.

There is a need to develop interventions to facilitate improved end of life care for this group. The systematic review I conducted highlighted the paucity of interventions in the ILD population which focus on symptom control and QoL outcomes. It also brings to the forefront issues which limit comparison across studies; there was a paucity of RCTs (all were published in the last 10 years), very few studies were powered for QoL or symptoms as primary outcome, there was poor reporting of data and mixed group studies did not report outcome measures separately. Despite some work at developing outcome scales specifically related to this disease group (254) (255, 256) I found poor use of validated outcome measures and a heterogeneity of measures used. Future areas of work which are needed include international consensus regarding patient reported outcome measures and study methodology to ensure that future trials capture accurate symptom control and QoL data.

Patients with IPF experience increased healthcare resource utilisation, and direct medical costs.(224) As the population gets older, we can expect that the burden on healthcare will increase.(224) Timely and adequate symptom control may prevent unnecessary hospital admissions and therefore contain some expenditure. Interestingly, the systematic review conducted showed that government funding provided only 6% of support for trials and over a quarter of studies had some source of industry funding. Studies which are funded by industry are unlikely to have symptoms and QoL as primary outcome measures. There also needs to be detailed health economic analysis accompanying interventional studies to assess the true impact of transferring the end of life management of these patients from the specialist to the community setting.

During the CC, for patients who wished to discuss PPD, no patient expressed hospital as their PPD. The actual place of death for patients having received the CC was hospital in only 28% of

patients. This is much less than found in a retrospective case note review (257) which found that 76% of PIF-ILD patients attending RBH and KCH in a one year period died in hospital. Patients with IPF experience increased healthcare resource utilisation, and direct medical costs.(224) This is especially important at the end of life. It is possible that the CC, through establishing links in the community setting and preventing crisis admissions, enabled patients to not die in hospital. The economic impact of this needs to be further investigated.

There is a need for these patients to have clear care planning and co-ordination of their care. As discussed in Chapter 5, it is not clear from this research how exactly the CC, as a complex intervention, delivered improvements in outcomes seen. Further research is needed to ascertain the active component. It is difficult to know whether the benefit from the intervention is due to the CC or palliative care involvement. Certainly patients who receive timely palliative care will have better co-ordination of services, symptom care, emotional support, education and family support and this is something that the H2H intervention facilitates. In developing understanding into the active ingredients in the H2H intervention, the CC needs to be examined more closely during delivery. Aspects which need to be considered include content of each CC, themes considered and the interaction with patients, informal caregivers and HPs. This may be done through quantitative or qualitative measures. This may provide valuable information on how the H2H intervention is working in the PIF-ILD setting and how and why this differs to the cancer setting or to normal specialist palliative care input.

In the Mitchell et al study (78), the CC was conducted between specialist palliative care teams and GPs via telephone. This study was conducted in the cancer group and patients and informal caregivers were not involved in the CCs. Telephone participation for GPs (rather than face-to-face participation) was felt to be a less successful form of communication when used in a RCT looking at case conferencing in Australia.(235) It is difficult to know whether this form of mode of delivery could be used in the PIF-ILD group effectively but warrants further investigation.

Further studies with larger samples of patients, informal caregivers and HPs across different sites are needed to assess the generalisability of the findings presented in this study. In addition, further studies would need to assess the longer term effects of the CC. It may be that a short term intervention early on in the disease process may be as beneficial as and more cost-effective than an intervention with follow up until death.

6.2.5 Personal reflection

This PhD has made me acutely aware of the far reaching impact of having unmet palliative care needs and how this impacts every part of patients' and informal caregivers' lives. Throughout this PhD I have been touched by how PIF-ILD patients and informal caregivers struggled in silence. They were unaware of services that were available to them and suffered without complaint. During data collection and the qualitative interviews conducted as part of the RCT, it became clear that these patients and informal caregivers were incredibly grateful for the support/services that they received from, and as a result of, the H2H intervention. This has made me aware that clinical services need to be directed at both the patient and the informal caregivers as this is a disease that effects every part of patients' and informal caregivers' lives. I believe that we have a duty to ensure that disease groups such as PIF-ILD receive an equitable share of resources and end of life provision including services that other disease groups, such as cancer and COPD, had been receiving for many years. I would hope that this PhD helps to highlight some of these issues and may facilitate development of services going forward.

Even though at times this PhD has been hard work and emotionally draining, I have experienced a great deal of personal enjoyment from the sustained contact over time with PIF-ILD patients and informal caregivers. I felt a genuine pleasure in learning of their disease experiences as well as feeling very privileged that participants felt able to 'open up to me' about intensely personal issues. I believe that my PhD has positively influenced my clinical practice through not only making me a better listener, as a result of skills acquired during qualitative interviewing, but also more considerate of informal caregivers and the far reaching and devastating impact that having an advanced disease with unmet need can have.

6.3 Conclusion

This mixed methods study to develop a complex intervention provides a major contribution towards the understanding of the palliative care needs of patients with PIF-ILD. It illustrates the high burden of the unmet symptom control and psychological needs experienced by these patients and how these patients and their informal caregivers are suffering in silence. PIF-ILD patients rarely receive adequate support in the community and they are not accessing community palliative care services. The adapted H2H intervention is innovative in this group in its attempt to improve symptom control, co-ordination of care and crisis management through a case conference model of care. The intervention involved patients, informal caregivers and HPs in a case conference focussing on addressing the patients' and informal caregivers' needs. Findings from this study suggest that that a case conference model of care for this group of patients and informal caregivers may improve palliative care needs, QoL and anxiety and depression. Further research is needed to evaluate these potential effects in a larger Evaluation trial.

As well as providing some of the very first evidence of the palliative care needs of these patients and informal caregivers, this study has also presented methodological contributions to research at the end of life in PIF-ILD. These include the successful use of mixed methods and the use of the Medical Research Council's guidance supported by the MOREcare guidance to develop a complex intervention at the end of life. The use of these methods is novel in this disease group. This study has shown that high quality research can be conducted at the end of life in PIF-ILD.

Definitions and Glossary

Acceptability- adequate to satisfy a need, requirement or standard

Attrition- decreasing sample size at subsequent assessment points due to drop-out or withdrawal.

Authenticity- the portrayal of research that reflects the meanings and experiences that are lived and perceived by the participants. (258)

Axiology- The philosophical study of value

Complementarity- the elaboration or enhancement of the results from one method with the results from another.

Complex Intervention- usually described as an intervention that contains several interacting components but other elements of complexity include difficulty of behaviours required by those delivering or receiving intervention, number of groups or organisational levels targeted by intervention, number and variability of outcomes and degree of flexibility or tailoring of the intervention permitted.(13)

Constant comparative method- ongoing reflection and analysis formalised in coding procedures with generation of categories. Ideas generated during reflection and analysis are subject to further comparisons.

Convergence- the tendency to become more alike over time.

Criticality- researchers' critical appraisal of every research decision.

Discrepancy- an instance of difference or inconsistency.

Divergence- difference or deviation.

Development- results from one method to help develop or inform the other method.

Epistemology- A justification of knowledge. (83)

Expansion- extending the breadth and range of enquiry by using different methods.

Feasibility study- aims to objectively and rationally uncover the strengths and weaknesses of an intervention, the resources required to carry through, and ultimately the prospects for success.

Framework analysis- an approach to analysis developed by the National Centre for Social Research, and explicitly geared towards findings orientated towards policy and practice.(101)
To describe the content of text or communication objectively, systematically and quantitatively. Stages include familiarisation, thematic analysis, indexing and charting.

Hypothesis- a testable proposition.(259)

IPF- Idiopathic pulmonary fibrosis (IPF) (previously known as cryptogenic fibrosing alveolitis or idiopathic fibrosing interstitial pneumonia) is a chronic, progressive form of lung disease characterised by fibrosis of lung parenchyma. Microscopically, lung tissue from patients shows a characteristic set of histologic/pathologic features known as usual interstitial pneumonia (UIP). The cause of IPF is unknown.(48)

ILD- Interstitial lung disease (ILD) describes a large group of acute and chronic lung disorders, with variable degrees of pulmonary inflammation most of which cause progressive scarring or fibrosis of lung parenchyma.(160)

Initiation- the recasting of questions or results from one method with questions or results from the other method.

Integrity- honesty and probity within the conduct of the research.

Intervention- any measure whose purpose is to improve health or alter the course of disease.

Member checking- method of enhancing credibility in qualitative data analysis through debriefings and discussions with interviewees.

Ontology- The science or study of being.

Paradigm- a set of ideas (hypotheses) about the phenomena under inquiry

PIF-ILD- a clinical diagnosis of Non-Specific Interstitial Pneumonia, Idiopathic Pulmonary Fibrosis or Idiopathic Interstitial Pneumonia or a histological diagnosis of UIP as classified by ATS/ERS criteria.(160)

Advanced PIF-ILD- Progressive Idiopathic Fibrotic Interstitial Lung Disease with TLCO (percentage transfer factor) <40% and deteriorating clinical condition.

Pilot studies- version of the main study that is run in miniature to test whether the components of the main study can all work together. It is focused on the processes of the main study, for example to ensure recruitment, randomisation, treatment, and follow-up assessments all run smoothly. It will therefore resemble the main study in many respects, including an assessment of the primary outcome.

Recruitment- process of screening and enrolling patients into clinical trials

Method- a specific research technique.(259)

Mixed methods research- mixed methods research has been defined as the use of two or more methods that draw on different meta-theoretical assumptions to address a research question.(260) As a method, it focuses on collecting, analysing, and mixing both quantitative and qualitative data in a single study or series of studies.

Model- an overall framework for looking at reality. (259)

Palliative Care- is an approach that improves the QoL of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual. It includes:

- a primary focus on QoL
- pro-active and detailed symptom management
- a patient and family-centred approach
- consideration of psycho-social and spiritual, as well as physical issues. (20)

Palliative ILD treatments- non-disease modifying treatments whose only goal is to improve symptoms and QoL e.g diamorphine.

Preferred Place of Care- where a patient would wish to be cared for in the last few days and weeks of life.

Preferred Place of Death- where a patient would wish to die.

Radical ILD treatments- disease modify treatments whose primary goal is to slow disease progression.

Respondent validation- cross-checking findings with respondents. Can help to refine explanations.

Triangulation- the use of three or more different research methods (i.e. multiple methods) to investigate the phenomenon of interest.

APPENDICES

APPENDIX A Ethics application, amendments and approvals

Notice of Amendment

28 MAY 2010

IRAS Version 2.5

09/ H0806/74 Am02

The integrated dataset required for your project will be created from the answers you give to the following questions. The system will generate only those questions and sections which (a) apply to your study type and (b) are required by the bodies reviewing your study. Please ensure you answer all the questions before proceeding with your applications.

Please enter a short title for this project (maximum 70 characters)
Quality of Life tools to assess Interstitial Lung Diseases and sarcoid

1. Is your project research?

☒ Yes ☐ No

2. Select one category from the list below:

- ☐ Clinical trial of an investigational medicinal product
- ☐ Clinical investigation or other study of a medical device
- ☐ Combined trial of an investigational medicinal product and an investigational medical device
- ☐ Other clinical trial or clinical investigation
- ☒ Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology
- ☐ Study involving qualitative methods only
- ☐ Study limited to working with human tissue samples, other human biological samples and/or data (*specific project only*)
- ☐ Research tissue bank
- ☐ Research database

If your work does not fit any of these categories, select the option below:

☐ Other study

2a. Please answer the following question(s):

- a) Does the study involve the use of any ionising radiation? ☐ Yes ☒ No
- b) Will you be taking new human tissue samples (or other human biological samples)? ☐ Yes ☒ No
- c) Will you be using existing human tissue samples (or other human biological samples)? ☐ Yes ☒ No

3. In which countries of the UK will the research sites be located? (Tick all that apply)

- ☒ England
- ☐ Scotland
- ☐ Wales
- ☐ Northern Ireland

3a. In which country of the UK will the lead NHS R&D office be located:

☒ England

☐ Scotland

- ☐ Wales
☐ Northern Ireland
☐ This study does not involve the NHS

4. Which review bodies are you applying to?

- ☒ NHS/HSC Research and Development offices
☐ Social Care Research Ethics Committee
☒ Research Ethics Committee
☐ National Information Governance Board for Health and Social Care (NIGB)
☐ Ministry of Justice (MoJ)

5. Will any research sites in this study be NHS organisations?

- ☒ Yes ☐ No

5a. Do you want your application to be processed through the NIHR Coordinated System for gaining NHS Permission?

- ☐ Yes ☒ No

If yes, you must complete and submit the NIHR CSP Application Form immediately after completing this project filter, before proceeding with completing and submitting other applications.

6. Do you plan to include any participants who are children?

- ☐ Yes ☒ No

7. Do you plan to include any participants who are adults unable to consent for themselves through physical or mental incapacity? *The guidance notes explain how an adult is defined for this purpose.*

- ☐ Yes ☒ No

8. Do you plan to include any participants who are prisoners or young offenders in the custody of HM Prison Service in England or Wales?

- ☐ Yes ☒ No

9. Is the study, or any part of the study, being undertaken as an educational project?

- ☐ Yes ☒ No

10. Is this project financially supported by the United States Department for Health and Human Services?

- ☐ Yes ☒ No

11. Will identifiable patient data be accessed outside the clinical care team without prior consent at any stage of the project (including identification of potential participants)?

- ☐ Yes ☒ No

Please use this form to notify the main REC of substantial amendments to all research other than clinical trials of investigational medicinal products (CTIMPs). For CTIMPs, please use the European Commission notice of substantial amendment form at <http://eudract.emea.europa.eu/document.html>. The form should be completed by the Chief Investigator using language comprehensible to a lay person. Support in principle should be sought from the study sponsor before the amendment is submitted.

Details of Chief Investigator:

Title	Forename/Initials Surname
Dr	Surinder Birring
Work Address	Department of Respiratory Medicine, King's College Hospital Denmark Hill, London
PostCode	SE5 9RS
Email	surinder.birring@kch.nhs.uk
Telephone	02032994630
Fax	

Full title of study:	Quality of Life Tools to assess Interstitial Lung Diseases and Sarcoidosis
Lead sponsor:	Kings College Hospital
Name of REC:	
REC reference number:	09/H0808/108
Name of lead R&D office:	Kings College Hospital
Date study commenced:	16 November 2009
Protocol reference (if applicable), current version and date:	version 3 dated 24/05/10
Amendment number and date:	2 25/05/10

Type of amendment

(a) Amendment to information previously given in IRAS

☒ Yes ☐ No

If yes, please refer to relevant sections of IRAS in the "summary of changes" below

(b) Amendment to the protocol

☒ Yes ☐ NoIf yes, please submit either the revised protocol with a new version number and date, highlighting changes in bold, or a document listing the changes and giving both the previous and revised text.

version 3- changes highlighted by underlining

(c) Amendment to the information sheet(s) and consent form(s) for participants, or to any other supporting documentation for the study

☒ Yes ☐ No

If yes, please submit all revised documents with new version numbers and dates, highlighting new text in bold. new information/consent sheets for carers and health professionals and for focus groups.

Is this a modified version of an amendment previously notified and not approved?

☐ Yes ☒ No

If yes, please explain the modifications made under "Summary of changes" below

Summary of changes

Briefly summarise the main changes proposed in this amendment. Explain the purpose of the changes and their significance for the study.

If the amendment significantly alters the research design or methodology, or could otherwise affect the scientific value of the study, supporting scientific information should be given (or enclosed separately). Indicate whether or not additional scientific critique has been obtained.

As part of our multi-disciplinary team discussion, it has become clear that we will need focus groups and carer interviews to inform us of any further areas that may be important. In addition, it has now been noted that as well as exploring the aspects of the disease which are most important to the patient, we believe that it would be important to assess current needs provision and how this impacts on quality of life. Therefore we would like to do the following in addition to the current semi-structured patient interviews:

(1) Semi-structured interviews with carers

- We will aim to interview 10 carers at King's College Hospital (KCH). 10 at Royal Brompton Hospital (RBH) initially.
- Interviews will continue until no new themes are emerging.

The schedule used will be similar to that used for patients with applicable adjustment.

(2) Semi-structured interviews with healthcare professionals and stakeholders (Previous ethics approval was for MDT discussion only)

- 5 interviews in total to be conducted of staff in primary care, respiratory medicine, palliative care and physiotherapy

(3) 4 focus groups-split between KCH and RBH (1 patient, 1 carer, 2 health professionals) each comprising 6-10 participants.

- Schedules as for the interviews will be used for the focus groups.

(4) Dr Sabrina Bajwah is to be added as a researcher. She is a Consultant in Palliative Medicine who is currently working as a research fellow at the Cicely Saunders Institute. She already holds an honorary contract at Royal Brompton Hospital and Kings College Hospital. A copy of her CV is enclosed.

Any other relevant information

Applicants may indicate any specific issues relating to the amendment, on which the opinion of a reviewing body is sought.

List of enclosed documents

Document	Version	Date
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4

30870/123603/13/810/2269/178060

Notice of Amendment

IRAS Version 2.5

Curriculum Vitae Dr Sabrina Bajwah ✓	1	10/05/2010
Participant Information Sheet-KCH Interviews ✓	3	24/05/2010
Participant Information Sheet-KCH Focus Groups ✓	3	24/05/2010
Participant Information Sheet-RBH Interviews ✓	2	24/05/2010
Participant Information Sheet RBH Focus Groups ✓	2	24/05/2010
Schedule for interview with carers ✓	1	24/05/2010
Schedule for interview with health professionals ✓	1	24/05/2010
Participant Consent form-KCH Patients ✓	2	24/05/2010
Participant Consent form-KCH non-Patients ✓	1	24/05/2010
Participant Consent form-RBH Patients ✓	2	24/05/2010
Participant Consent form-RBH non-Patients ✓	1	24/05/2010
Protocol ✓	3	24/05/2010

Declaration by Chief Investigator

1. I confirm that the information in this form is accurate to the best of my knowledge and I take full responsibility for it.
2. I confirm that the study sponsor has been notified of the proposed amendment.
3. I consider that it would be reasonable for the proposed amendment to be implemented.

Date: _____



National Research Ethics Service

South West London REC 4

St Georges University of London
South London REC Office 1
Corridor 1 - Room 1.13
1st Floor, Jenner Wing
Tooting
London
SW17 0RE

Tel: 020 7188 2259
Fax: 020 7188 2258

10 June 2010

Dr Surinder Birring
Consultant Respiratory Physician and Honorary Senior Lecturer
King's College Hospital
Department of Respiratory Medicine
Denmark Hill
London SE5 9RS

Dear Dr Birring

Study title: Quality of Life Tools to assess Interstitial Lung Diseases and Sarcoidosis
REC reference: 09/H0806/74
Protocol number: 3
Amendment number: AM02
Amendment date: 25 May 2010

Ethical opinion

Favourable Opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Interview Schedules/Topic Guides	1	25 May 2010
Participant Consent Form: RBH Non-Patients	3	09 June 2010
Participant Consent Form: RBH Patients	3	09 June 2010
Participant Consent Form: KCH Non-Patients	4	09 June 2010
Participant Consent Form: KCH Patients	4	09 June 2010
Participant Information Sheet: KCH Interviews	4	09 June 2010
Participant Information Sheet: KCH Focus Groups	4	09 June 2010
Participant Information Sheet: RBH Interviews	3	09 June 2010
Participant Information Sheet: RBH Focus Group	3	09 June 2010
Investigator CV	1	10 May 2010
Protocol	3	25 May 2010

This Research Ethics Committee is an advisory committee to London Strategic Health Authority
The National Research Ethics Service (NRES) represents the NRES Directorate within
the National Patient Safety Agency and Research Ethics Committees in England

Notice of Substantial Amendment (non-CTIMPs)	1.0	25 May 2010
Interview Schedules/Topic Guides	1	25 May 2010

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

09/H0806/74:	Please quote this number on all correspondence
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Yours sincerely



Samantha Roper
Committee Co-ordinator

E-mail: samantha.roper@gstt.nhs.uk

Enclosures: List of names and professions of members who took part in the review

Copy to:

Sponsor / R&D

Miss Jamie Peterson
King's College Hospital
R&D Department
34 Love Walk
London SE5 8AD

Dr Amit Suresh Patel
Department of Respiratory Medicine
King's College Hospital
Denmark Hill
London SE5 9RS

Dr Sabrina Bajwah
38c Tremadoc Road
Clapham
London SW4 7LL

*The National Research Ethics Service (NRES) represents the NRES Directorate within
the National Patient Safety Agency and Research Ethics Committees in England*

South West London REC 4

Attendance at PRS Sub-Committee of the REC meeting on 09 June 2010

Name	Profession	Capacity
Mrs Wendy Brooks	Stroke Nurse Consultant	Expert
Mr Derek Cock	Chief Pharmacist	Expert
Mrs Anne Laurie	Lecturer in Clinical Communications	Lay
Canon Christopher Vallins	Regional Chaplaincy Adviser	Lay

Also in attendance:

Name	Position (or reason for attending)
Ms Samantha Roper	Proportionate Review Service Coordinator

The National Research Ethics Service (NRES) represents the NRES Directorate within the National Patient Safety Agency and Research Ethics Committees in England

Welcome to the Integrated Research Application System

IRAS Project Filter

The integrated dataset required for your project will be created from the answers you give to the following questions. The system will generate only those questions and sections which (a) apply to your study type and (b) are required by the bodies reviewing your study. Please ensure you answer all the questions before proceeding with your applications.

Please enter a short title for this project (maximum 70 characters)
H2H PIF-ILD study

1. Is your project research?

☒ Yes ☐ No

2. Select one category from the list below:

- ☐ Clinical trial of an investigational medicinal product
- ☐ Clinical investigation or other study of a medical device
- ☐ Combined trial of an investigational medicinal product and an investigational medical device
- ☐ Other clinical trial or clinical investigation
- ☒ Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology
- ☐ Study involving qualitative methods only
- ☐ Study limited to working with human tissue samples, other human biological samples and/or data (*specific project only*)
- ☐ Research tissue bank
- ☐ Research database

If your work does not fit any of these categories, select the option below:

☐ Other study

2a. Please answer the following question(s):

- a) Does the study involve the use of any ionising radiation? ☐ Yes ☒ No
- b) Will you be taking new human tissue samples (or other human biological samples)? ☐ Yes ☒ No
- c) Will you be using existing human tissue samples (or other human biological samples)? ☐ Yes ☒ No

3. In which countries of the UK will the research sites be located? (*Tick all that apply*)

- ☒ England
- ☐ Scotland
- ☐ Wales
- ☐ Northern Ireland

3a. In which country of the UK will the lead NHS R&D office be located:

- ☒ England
- ☐ Scotland

- ☐ Wales
☐ Northern Ireland
☐ This study does not involve the NHS

4. Which review bodies are you applying to?

- ☒ NHS/HSC Research and Development offices
☐ Social Care Research Ethics Committee
☒ Research Ethics Committee
☐ National Information Governance Board for Health and Social Care (NIGB)
☐ Ministry of Justice (MoJ)
☐ National Offender Management Service (NOMS) (Prisons & Probation)

5. Will any research sites in this study be NHS organisations?

- ☒ Yes ☐ No

5a. Do you want your application to be processed through the NIHR Coordinated System for gaining NHS Permission?

- ☒ Yes ☐ No

If yes, you must complete and submit the NIHR CSP Application Form immediately after completing this project filter, before proceeding with completing and submitting other applications.

6. Do you plan to include any participants who are children?

- ☐ Yes ☒ No

7. Do you plan at any stage of the project to undertake intrusive research involving adults lacking capacity to consent for themselves?

- ☐ Yes ☒ No

Answer Yes if you plan to recruit participants aged 16 or over who lack capacity, or to retain them in the study following loss of capacity. Intrusive research means any research requiring consent in law. This includes use of identifiable tissue samples or personal information, except where application is being made to the NIGB Ethics and Confidentiality Committee to set aside the common law duty of confidentiality in England and Wales. Please consult the guidance notes for further information on the legal frameworks for research involving adults lacking capacity in the UK.

8. Do you plan to include any participants who are prisoners or young offenders in the custody of HM Prison Service or who are offenders supervised by the probation service in England or Wales?

- ☐ Yes ☒ No

9. Is the study, or any part of the study, being undertaken as an educational project?

- ☒ Yes ☐ No

9a. Is the project being undertaken in part fulfilment of a PhD or other doctorate?

- ☒ Yes ☐ No

10. Will this research be financially supported by the United States Department of Health and Human Services or any of its divisions, agencies or programs?

☐ Yes ☒ No

11. Will identifiable patient data be accessed outside the clinical care team without prior consent at any stage of the project (including identification of potential participants)?

☐ Yes ☒ No

Integrated Research Application System
Application Form for Research administering questionnaires/interviews for quantitative analysis or mixed methodology study



Application to NHS/HSC Research Ethics Committee

The Chief Investigator should complete this form. Guidance on the questions is available wherever you see this symbol displayed. We recommend reading the guidance first. The complete guidance and a glossary are available by selecting [Help](#).

Please define any terms or acronyms that might not be familiar to lay reviewers of the application.

Short title and version number: (maximum 70 characters - this will be inserted as header on all forms)
H2H PIF-ILD study

Please complete these details after you have booked the REC application for review.

REC Name:
London Chelsea

REC Reference Number:
11/LO/0999

Submission date:
14/06/2011

PART A: Core study information

1. ADMINISTRATIVE DETAILS

A1. Full title of the research:

A fast track randomised controlled trial to evaluate a Hospital2Home palliative care service for patients with advanced Progressive Idiopathic Fibrotic Interstitial Lung Disease

A2-1. Educational projects

Name and contact details of student(s):

Student 1

	Title	Forename/Initials	Surname
	Dr	Sabrina	Bajwah
Address	Department of Palliative Medicine Royal Marsden Hospital Fulham Rd		
Post Code	SW3 6JJ		
E-mail	sabrina.bajwah@kcl.ac.uk		

Telephone 02078082761

Fax 02078118132

Give details of the educational course or degree for which this research is being undertaken:

Name and level of course/degree:

Ph.D

Name of educational establishment:

King's College London

Name and contact details of academic supervisor(s):

Academic supervisor 1

	Title	Forename/Initials	Surname
	Professor	Irene J	Higginson
Address	Cicely Saunders Institute		
	Bessemer Rd		
	Denmark Hill		
Post Code	SE5 9RJ		
E-mail	Irene.Higginson@kcl.ac.uk		
Telephone	020 7848 5516		
Fax	020 7848 5517		

Academic supervisor 2

	Title	Forename/Initials	Surname
	Dr	Julia	Riley
Address	Department of Palliative Medicine		
	Royal Marsden Hospital		
	Fulham Rd		
Post Code	SW3 6JJ		
E-mail	julia.riley@rmh.nhs.uk		
Telephone	020 7808 2761		
Fax	020 7811 8132		

Academic supervisor 3

	Title	Forename/Initials	Surname
	Professor	Athol U	Wells
Address	Interstitial Lung Disease Unit, Emmanuel Kaye Building,		
	Manresa Rd		
	Chelsea		
Post Code	SW3 6LR		
E-mail	athol.wells@rbht.nhs.uk		
Telephone	020 7351 8327		
Fax			

Academic supervisor 4

Title	Forename/Initials	Surname
-------	-------------------	---------

Address	Dr Jonathan Koffman Cicely Saunders Institute Bessemer Rd Denmark Hill
Post Code	SE5 9RJ
E-mail	jonathan.koffman@kcl.ac.uk
Telephone	020 7848 5516
Fax	020 7848 5517

Please state which academic supervisor(s) has responsibility for which student(s):
Please click "Save now" before completing this table. This will ensure that all of the student and academic supervisor details are shown correctly.

Student(s)	Academic supervisor(s)
Student 1 Dr Sabrina Bajwah	<input type="checkbox"/> Dr Julia Riley <input type="checkbox"/> Professor Irene J Higginson <input type="checkbox"/> Professor Athol U Wells <input checked="" type="checkbox"/> Dr Jonathan Koffman

A copy of a current CV for the student and the academic supervisor (maximum 2 pages of A4) must be submitted with the application.

A2-2. Who will act as Chief Investigator for this study?

- ☐ Student
☒ Academic supervisor
☐ Other

A3-1. Chief Investigator:

	Title Forename/Initials Surname
	Dr Julia Riley
Post	Consultant and Head of Palliative Care Department
Qualifications	MRCGP, FRCP, MD
Employer	Royal Marsden Hospital NHS Trust
Work Address	Department of Palliative Medicine Royal Marsden Hospital Fulham Rd
Post Code	SW3 6JJ
Work E-mail	julia.riley@rmh.nhs.uk
* Personal E-mail	
Work Telephone	02078082761
* Personal Telephone/Mobile	
Fax	02078118132

* This information is optional. It will not be placed in the public domain or disclosed to any other third party without prior consent.

A copy of a current CV (maximum 2 pages of A4) for the Chief Investigator must be submitted with the application.

A4. Who is the contact on behalf of the sponsor for all correspondence relating to applications for this project?
This contact will receive copies of all correspondence from REC and R&D reviewers that is sent to the CI.

	Title Forename/Initials Surname
	Ms Jane Lawrence
Address	Royal Marsden Hospital Downs Rd Sutton
Post Code	SM2 5PT
E-mail	jane.lawrence@rmh.nhs.uk
Telephone	020866 13909
Fax	

A5-1. Research reference numbers. Please give any relevant references for your study:

Applicant's/organisation's own reference number, e.g. R & D (if available):

Sponsor's/protocol number:

Protocol Version: 1.3

Protocol Date: 12/05/2011

Funder's reference number:

International Standard Randomised Controlled Trial Number (ISRCTN): N/A

ClinicalTrials.gov Identifier (NCT number): N/A

European Clinical Trials Database (Eudra CT) number: N/A

Project website: N/A

Ref.Number	Description	Reference Number
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A5-2. Is this application linked to a previous study or another current application?

☐ Yes ☒ No

Please give brief details and reference numbers.

2. OVERVIEW OF THE RESEARCH

To provide all the information required by review bodies and research information systems, we ask a number of specific questions. This section invites you to give an overview using language comprehensible to lay reviewers and members of the public. Please read the guidance notes for advice on this section.

A6-1. Summary of the study. Please provide a brief summary of the research (maximum 300 words) using language easily understood by lay reviewers and members of the public. This summary will be published on the website of the National Research Ethics Service following the ethical review.

Interstitial Lung Disease (ILD) is a lung condition characterised by progressive scarring - known as fibrosis. This is especially seen in patients with idiopathic pulmonary fibrosis (IPF). There are around 2,000 new patients diagnosed in the UK every year with a similar number of deaths.

Fibrotic-ILD causes breathing to slowly deteriorate and as there is no cure, an estimated two-thirds of patients die within five years of diagnosis. Patients suffer from many symptoms including shortness of breath, cough, low mood and fatigue which are currently being poorly managed. In addition, these patients suffer a poor health related quality of life whilst dying from their disease.

In the later stages of their disease, these patients often end up in hospital (see appendix 1a) when there is no proven or effective treatment. Many die there despite wishing to be looked after and die at home. These patients rarely receive

palliative care which may help to improve their symptoms, quality of life, address end of life planning needs and prevent hospital admission. The Hospital2Home case conference conducted in the patient's home (or place of their choice) aims to address this. At the case conference involving the patient, their carers, a specialist nurse, and all the community health professionals, a care plan specific to the patient will be developed. Each health professional will be aware of their responsibility and duties. We will look at whether this results in better symptom control and better quality of life for the patient and their carer. We will also examine whether this prevents emergency hospital admission and allows patients to die in their preferred place. We will compare patients who receive the service immediately with those who receive it after a delay.

A6-2. Summary of main issues. Please summarise the main ethical and design issues arising from the study and say how you have addressed them.

We have decided on a fast-track randomised controlled trial design as it allows us the robustness of a randomised controlled trial but ensures that every participant will receive the service within the time period of the trial. This may be after a slight delay but it ensures that we are not enrolling palliative care patients into a study where they do not receive the intervention at all. In addition, we hope this will improve our recruitment to the study. Patients who do not wish to take part in the study will not be offered the Hospital2Home (H2H) case conference and they will continue to receive standard care.

It has been well documented that research in palliative care, and in particular end of life is a challenge. However research at the end of life should not be thought of as a special case as these challenges are equally relevant in other areas of research. All research needs sensitivity, caution, and respect for the physical and emotional wellbeing of participants. The main ethical issues related to this study are hinged on the arguments between protecting vulnerable adults from research exploitation and empowering participants to maintain autonomy in the context of a research study. This study does deal with two particularly vulnerable groups. All the patients entered into the study are by entry criteria in the last year of life. They, and their informal caregivers may be under more stress as a result of this, and may also feel dependent on their clinical teams to manage any complex symptoms/psychological/social issues they may have. All patients and carers attending outpatients or on the ward, will be assessed for eligibility by the clinical team (either the respiratory/palliative care teams).

Those patients and informal caregiver who meet the study inclusion criteria will be informed about the study, and given an information sheet. If they are interested, and with their agreement their names and contact telephone number will then be passed onto the research team. This method of identification has been chosen to limit coercion, as the clinical team is entirely separate from the research team and therefore participants should not feel pressured to enter the study.

Possible harm could be caused to the patient if they are not aware that their lung disease is terminal in nature. A clear assessment of the patient's information needs will need to be carried out at the initial assessment. The research team will not force information on the patient if they do not wish to discuss end of life planning/advance care planning needs at the case conference. In this instance, it will be noted that the patient does not want to discuss this area and a separate conversation will occur between the health professionals +/- informal caregiver (with the patients permission). However, the case conference will still occur and a care plan drawn up.

Patients in the last week of life will be excluded as we deem a case conference as too burdensome in this group.

Non English speaking patients have been excluded as the data collection will be through face to face interviews and telephone questionnaires with the co-investigators (and anyone they supervise) who are English speaking, and case conferences are currently only held in English.

Consent

All members of the research team are able to assess capacity and understand the principles of informed consent. No research will be conducted without informed consent.

The initial approach to potential participants will be by the clinical teams as described above. At this contact potential participants will be given an information sheet and verbal consent obtained for the research team to make contact. Where possible, participants will be given sufficient time to consider entering the study (at least 24 hours), and will also be encouraged to discuss the study with their family.

If they agree to enter, the researcher will check the participant and informal caregivers understanding of the information sheet, answer any questions they may have about participation. The participant and informal caregiver will then be asked to complete a written consent form, and a copy of this will be given to the patient and carer, stored in their medical notes, the clinical record file and the research site file (appendix 6&7).

It will be expressed upon the informal caregiver that if the participant agrees to enter the study the informal caregiver is under no obligation to, and a decision not to will not affect the patient's care or their future care in any way.

Both can withdraw, with or without the other, at anytime and do not need to give a reason

This is a longitudinal study and therefore at each contact the validity of the initial consent from participants will be reconfirmed.

Risks, burdens and benefits:

Previous studies have shown that cancer patients approaching the end of life can feel positive towards participating in studies. Perceived benefits from participation in this study are similar to those previously documented in palliative care research, namely increased monitoring and attention for the participants themselves, and altruistic motives of improving care for others.

Contact overtime through serial interviews may be important, and a positive experience rather than a burden, for those whose active treatment and follow up has ceased.

All the questionnaires being used are validated tools, and have been previously tested on populations similar to the study population. However, it is recognised that the completion of such questionnaire tools may for some participants or informal caregivers cause distress or unmask psychological states of concern. After any interview adequate time will be allowed to check the impact and effect of the interview on the interviewee. They will also be directed to the appropriate source of health/social care professional as necessary. If necessary, the researcher will provide the interviewee with relevant information about local counselling services, and with the interviewee's consent inform their GP/community medical teams of any concerns. If the researcher has a high level of concern about the participant after the interview this will be urgently discussed with the principal investigator, and the clinical team to decide the most appropriate course of action.

All concerns of this nature will be documented in the clinical record file for the patient or carer, and the frequency of these concerns audited.

Confidentiality

All data relating to the study will be treated as confidential. All data from the study will be handled in accordance to trust policy and the Data Protection Act 1998. Data will be accessed and stored according to Caldicott Principles.

The record forms will be anonymised and kept in locked secure cupboards. Computer generated files will be backed up according to The Royal Marsden Hospital back up policy. The record and computer files will be kept for a minimum of 5 years.

Conflict of interest

The clinical team will be responsible for the medical care. They will not be involved in the study, other than identifying patients to be approached by the research team. The co-investigators (and anyone they supervise) and H2H research nurse will be responsible for the assessment process the H2H nurse will be responsible for the delivery of the H2H conference and the researchers responsible for the assessment process. The research team will not be involved in the clinical treatment of the patient population.

End of Study:

For the individual patient, the study ends when they withdraw, become too unwell to participate in serial interviews, complete all contacts in follow up or they die. For the informal caregiver, the study ends when they themselves decide to withdraw, they complete all follow up or they die.

A10. What is the principal research question/objective? *Please put this in language comprehensible to a lay person.*

What is the impact of the H2H intervention on symptom control in PIF-ILD patients in the last year of life compared to standard best practice?

A11. What are the secondary research questions/objectives if applicable? *Please put this in language comprehensible to a lay person.*

To assess whether H2H improves quality of life, informal caregiver burden, use and costs of formal health and social care services and prognosis.

To determine whether H2H allows people to achieve their preferred place of care and death.

To evaluate evidence based guidelines for the palliative management of patients with severe PIF-ILD.

To evaluate clinical use of a new staging system to identify patients with PIF-ILD for whom proactive planning of end-of life care is now appropriate

A12. What is the scientific justification for the research? *Please put this in language comprehensible to a lay person.*

In the later stages of their disease, PIF-ILD patients often end up in hospital when there is no proven or effective treatment. Many die there despite wishing to be looked after and die at home. These patients rarely receive palliative care which may help to improve their symptoms, quality of life and prevent hospital admission. The Department of Health has recommended looking at ways in which we can allow more people to be looked after and die where they wish to. Previous work in Australia has indicated that a case-conference model may help this process. However, there has been no similar work in this group of patients and there has not been any work looking at this model of care in the UK.

In recent months we have been conducting a review of the literature and interviews of patients, carers and health professionals. This has enabled us to start developing evidenced based guidelines for the management of the physical, psychological, spiritual and end of life-planning needs for these patients. These guidelines (still under development) will be used in the H2H case conference.

A13. Please summarise your design and methodology. *It should be clear exactly what will happen to the research participant, how many times and in what order. Please complete this section in language comprehensible to the lay person. Do not simply reproduce or refer to the protocol. Further guidance is available in the guidance notes.*

Design

A fast track pragmatic randomised controlled trial evaluating a H2H intervention for patients with severe PIF-ILD. (see Appendix 1b)

Setting

Royal Brompton Hospital (RBH) in-patient and out-patient units.

Recruitment, consent and randomisation

Patients will be identified by the respiratory and palliative care teams. After providing consent and baseline interview, patients meeting inclusion criteria will be allocated to fast track or waiting list by independent off-site randomisation. If patients are randomised to fast-track, their information will be passed to the H2H nurse to organise a case conference within one week of discharge. If patients are in the control arm, they will continue to receive Standard Best Practice (SBP) and their data will be held by the researcher until after the second interview (4 weeks). After this time, they will be contacted by the H2H nurse to receive the intervention and will be interviewed and followed up as for the fast track group.

All patients (in both groups) will have information collected at baseline, 4 weeks and 8 weeks after randomisation. The H2H case conference will occur where possible within a week of the baseline interview for the intervention group and within a week of the 4 week information collection for the waiting list group. Each patient will then be followed to the point of death to document place of death.

If the patient does not wish to enter the trial, they will not receive the H2H intervention. If staff screening the referral deem that the patient has urgent needs (the patient is in the last few days of life), then the patient will not enter the trial.

Standard best practice (SBP)

Patients affected by PIF-ILD within the study area receive a range of services. These are available to all those who receive the H2H intervention immediately or after a delay. Services include general practitioners, physiotherapy and respiratory services (including specialist rehabilitation services) and community palliative care teams. All will have seen a respiratory physician at RBH preceding referral and will remain under their care with access to in-patient care as appropriate.

The Hospital2Home Service (H2H): the intervention

H2H will be offered in addition to the SBP services outlined above. H2H aims to complement the existing local services and not to duplicate or replace them. This intervention is a new multiprofessional, patient centred meeting or case conference that is organised for people nearing the end-of-life. In recent months we have been conducting a review of the literature and interviews of patients, informal caregivers and health professionals. This has enabled us to start developing evidenced based guidelines for the management of the physical, psychological, spiritual and end of life-planning needs for these patients. These guidelines (still under development) will be used in the H2H case conference. The written guidelines will act as a supplement to the actual assessment. With the patients consent, a case conference will be organised in their home (or place of their choice). The patient, informal caregiver, H2H CNS, GP, district nurse, social worker and community palliative care nurse are invited to attend. Current and anticipated care needs are discussed, and an action plan is agreed allocating a responsible health care professional for each item. During the case conference, individualised care plans will be made. The care plan provides a quality comprehensive Palliative Care assessment (appendix 2). This is then communicated with local services, both primary and specialist teams resulting in streamlining of transfer of data and codifying responsibility for the patient, hospital and community

care professionals. The aim is to enable improved symptom control, quality of life, crisis prevention and decreased hospital admissions. In addition, this intervention will aim to manage uncertainty by facilitating early discussion about disease progression, improving communication and addressing end of life planning needs. The Royal Brompton Marie Curie H2H CNS will deliver teaching on the use of the evidence-based guidelines and will follow up each case conference to assure quality and control of the care received. The guidelines will permit a structured and evidence based practice in delivering palliative care where there has previously been none. The ongoing palliative care of these patients will be delivered by the community palliative care team as deemed appropriate by them.

Outcome measurements

For the individual patient, the study ends when they withdraw, become too unwell to participate in serial interviews, complete all contacts in follow up or they die. For the informal caregiver, the study ends when they themselves decide to withdraw, they complete all follow up or they die. If any participant becomes too unwell and unable to complete assessment, loses capacity or dies, they will be removed from the study. If the intervention has been delivered and the patient has become too unwell to continue in the study, consent will be reconfirmed with the informal caregiver and data will continue to be collected until the patient dies.

All patients (in both groups) will have information collected at baseline, 4 weeks and 8 weeks after randomisation. The H2H case conference will occur within a week of the baseline interview for the intervention group and within a week of the 4 week information collection for the waiting list group. Each patient will then be followed to the point of death to document place of death.

Primary outcome

The primary outcome will be a comparison of baseline versus week 4 symptom control and palliative concerns scored using the Palliative Care Outcome Scale (POS) (appendix 11), which comprises eight questions on anxiety, patient and informal caregiver concerns, and practical needs, each rated 0-4. This will ensure that there is ongoing data available if the patient becomes unwell and is no longer able to complete the study. We will compare the patient and carer POS in this study to see how inter-changeable the 2 assessments are.

Secondary outcomes

Secondary outcomes will focus on quality of life. (appendix 3) At each interview, service use questions will be asked which will record the frequency and types of health/social services received (see appendix 4, 12 & 13) in order that an accurate evaluation of cost of care per patient can be made. In addition semi-structured qualitative interviews will be conducted with patients, informal caregivers and health professionals. Prompts will include views of the case conference, the guidelines and what level of input was needed after the case conference. A record will be made of when and where the patient dies.

Other data collected

Face-to-face interviews with patients and informal caregivers, supplemented by hospital notes will be used to obtain demographic information such as age, sex, ethnicity, co-morbidity and duration of illness. This will allow the study population to be accurately described, enabling later assessment of applicability of the data to other populations and settings.

A14-1. In which aspects of the research process have you actively involved, or will you involve, patients, service users, and/or their carers, or members of the public?

- ☒ Design of the research
- ☒ Management of the research
- ☐ Undertaking the research
- ☐ Analysis of results
- ☒ Dissemination of findings
- ☐ None of the above

Give details of involvement, or if none please justify the absence of involvement.

We have a Project Advisory Group and a patient with Interstitial Lung Disease forms part of that group. He has been involved in the design of the research and will be involved in the management of the research and future dissemination of findings.

Advice and feedback from the patient representatives will be viewed of high importance, and research procedures will be constantly reassessed and adapted on the basis of this feedback.

Any patient/informal caregiver involved in the study will be offered a copy of the study results, and these will also be accessible to other patients groups within the Royal Marsden Hospital and Royal Brompton Hospital.

4. RISKS AND ETHICAL ISSUES

RESEARCH PARTICIPANTS

A17-1. Please list the principal inclusion criteria (list the most important, max 5000 characters).

Inclusion criteria

Patients

i) Clinical diagnosis of progressive fibrotic interstitial lung disease and a 30% survival at 1 year according to the validated prognostic tool developed by Professor Wells. (Appendix 5)

ii) Aged 18 years or over

iii) Any patient who does not meet any of the exclusion criteria

Carers

i) The informal caregivers of patients specified above, who can be significant others, relatives, friends or neighbours

ii) Aged 18 years or over

iii) Any carer who does not meet the exclusion criteria

Health Professional

Primary health professional in contact with patient able to give consent

A17-2. Please list the principal exclusion criteria (list the most important, max 5000 characters).

Exclusion criteria

Patients/informal caregiver

i) Any patient/informal caregiver unable to give informed consent

ii) Any patient/informal caregiver less than 18 years of age

iii) Participants who are unable to understand/speak English

iv) Participants who are remaining as an inpatient in the hospital or being transferred to another inpatient facility (eg hospice unit, for terminal care).

v) Participants whose prognosis is less than 1 week or judged too unwell to take part in serial interviews

RESEARCH PROCEDURES, RISKS AND BENEFITS

A18. Give details of all non-clinical intervention(s) or procedure(s) that will be received by participants as part of the research protocol. These include seeking consent, interviews, non-clinical observations and use of questionnaires.

Please complete the columns for each intervention/procedure as follows:

1. Total number of interventions/procedures to be received by each participant as part of the research protocol.
2. If this intervention/procedure would be routinely given to participants as part of their care outside the research, how many of the total would be routine?
3. Average time taken per intervention/procedure (minutes, hours or days)
4. Details of who will conduct the intervention/procedure, and where it will take place.

Intervention or procedure	1	2	3	4
Seeking Consent	2	0	20 min	Each eligible patient and their informal caregiver will be given an information sheet (appendix 6) by their clinical team to read and asked permission for the researcher to contact them to discuss the trial in more detail. The researcher will contact the participant, and if they agree to participate the researcher will ensure they understand the study in full along with their commitment, and then arrange a mutually convenient time and place for the first assessment. At the first assessment consent will be reconfirmed and the participants will be asked to complete a written consent form (appendix 7)
Face to Face	3	0	45 mins	This will be carried out by research team members who

interview			are trained in GCP, and will occur in a place convenient to the participant. Most of the questionnaires are validated, except for the health economic data collection tool and the questions about the Hospital2Home service itself which have been designed by the palliative care research team
Telephone Interview	2	0 30 minutes	Baseline interviews will always be conducted in person. However, follow up interviews may be conducted via telephone.
qualitative interviews	1	0 30-40 mins	As part of our mixed methods study, we will be conducting semi-structured in-depth interviews with an initial 5 patients, 5 informal caregivers and 5 health professional involved in the study. A topic guide looking at views of the H2H model of care will be used (appendix 4, 12 & 13)

A21. How long do you expect each participant to be in the study in total?

Each participant will be in the RCT for a maximum of 8 weeks. Patients, informal caregivers and health professionals will then be followed up with qualitative interviews. The participants will not be interviewed further after this but there will be a non-interventional follow up to note the place of death of the patient. Most patients will be expected to die within one year.

A22. What are the potential risks and burdens for research participants and how will you minimise them?

For all studies, describe any potential adverse effects, pain, discomfort, distress, intrusion, inconvenience or changes to lifestyle. Only describe risks or burdens that could occur as a result of participation in the research. Say what steps would be taken to minimise risks and burdens as far as possible.

Interviews with patients can be tiring and burdensome if they are medically unwell.

Therefore, the interview length in this study is a maximum of 45 minutes.

The interviews will be organised at a time and location convenient to the patient and can be stopped at any time if they are not keen to proceed. Any interview can be split into two parts over two consecutive days if the participants prefer.

End of life is a sensitive issue and it is recognised that the completion of questionnaire tools may for some participants or carers cause distress. After any interview adequate time will be allowed to check the impact and effect of the interview on the interviewee.

They will also be directed to the appropriate source of health/social care professional as necessary.

If necessary, the researcher will provide the interviewee with relevant information about local counselling services, and with the interviewee's consent inform their GP/community medical teams of any concerns.

If the researcher has a high level of concern about the participant after the interview this will be urgently discussed with the principle investigator, and the clinical team to decide the most appropriate course of action.

A23. Will interviews/questionnaires or group discussions include topics that might be sensitive, embarrassing or upsetting, or is it possible that criminal or other disclosures requiring action could occur during the study?

☒ Yes ☐ No

If Yes, please give details of procedures in place to deal with these issues:

It is possible that patients may not wish to discuss end of life planning issues and this may distress them. However, at the baseline interview, the patient's and informal caregivers information needs will be assessed and if the patient or informal caregiver do not wish to discuss prognosis or end of life/advance planning issues at the H2H case conference, this will be done separately between the health professionals.

However, end of life issues are sensitive and can be upsetting, and it is recognised that the completion of such questionnaire tools may for some participants or carers cause distress. Therefore, after any interview adequate time will be allowed to check the impact and effect of the interview on the interviewee. They will also be directed to the appropriate source of health/social care professional as necessary.

If necessary, the researcher will provide the interviewee with relevant information about local counselling services, and with the interviewee's consent inform their GP/community medical teams of any concerns.

If the researcher has a high level of concern about the participant after the interview this will be urgently discussed with the principle investigator at that site, and the clinical team to decide the most appropriate course of action.

All concerns of this nature will be documented in the clinical record file for the patient or carer, and the frequency of these concerns audited

A24. What is the potential for benefit to research participants?

Previous studies have shown that palliative care patients approaching the end of life can feel positive towards participating in observational studies (1). Perceived benefits from participation in this study are similar to those previously documented in palliative care research, namely increased monitoring and attention for the participants themselves, and altruistic motives of improving care for others (2,3). With reference to this being a longitudinal study with serial contacts Shipman et al (4) observed that contact overtime through serial interviews appeared to be important, and a positive experience rather than a burden, for those whose active treatment and follow up has ceased. Participants will be given the opportunity to express their views on the quality of end-of-life care.

- (1) Williams CJ, Shuster et al Interest in research participation among hospice patients, caregivers and ambulatory senior citizens: practice barriers or ethical constraints. *J Palliative Medicine* 2006;9:689-74
 (2) Ling J, Ress E et al What influences participation in clinical trials in palliative care in a cancer centre. *European Journal of Cancer* 2000;36:621-626
 (3) Ross C, Comblett M Attitudes of patients and staff to research in a specialist palliative care unit. *Palliative Medicine* 2003;17:491-497
 (4) Shipman C, Hotopf M et al The views of patients with advanced cancer regarding participation in serial questionnaire studies. *Palliative Medicine* 2008;22:913-920

A26. What are the potential risks for the researchers themselves? (if any)

The H2H nurse and other researchers will visit the patient and informal caregivers in their home. Any researcher visiting the patient's home will inform administrative staff before attending and leaving. All appointments and addresses will be documented clearly in the research office. Each researcher will have access to a mobile phone which will be kept on at all times.

It is recognised that, in end of life care, research staff can experience similar 'burn out' to clinical staff, and the stress of interviewing terminally ill patients, observing their decline and eventual death builds up over time. Therefore, monthly team meetings will be scheduled so staff can reflect and share concerns, and the research staff with direct participant contact will attend training on selfcare and will have access to additional professional support if needed.

RECRUITMENT AND INFORMED CONSENT

In this section we ask you to describe the recruitment procedures for the study. Please give separate details for different study groups where appropriate.

A27-1. How will potential participants, records or samples be identified? Who will carry this out and what resources will be used? For example, identification may involve a disease register, computerised search of GP records, or review of medical records. Indicate whether this will be done by the direct healthcare team or by researchers acting under arrangements with the responsible care organisation(s).

Patients will be identified via the respiratory and palliative care teams at the Royal Brompton.

There will be three groups of participants

- (1) Patients
- (2) Informal Carers
- (3) Community Health Care Professionals

(1) Patients will be identified by the clinical teams (the clinical respiratory and palliative care teams at the Royal Brompton Hospital). This will be done on ward rounds or reviewing patients and via clinic lists in outpatients.

(2) Informal Caregivers will be identified by the patient at the time when the clinical team gives the patient the information sheet about the study. The patients will be asked to name the person who spends most time with them and provides most of their daily care and support.

(3) Community Health Care Professionals will be identified by either their attendance at the H2H case conference or by the researcher asking the patient and informal caregiver to name the doctors and nurses that care for them whilst at home.

A27-2. Will the identification of potential participants involve reviewing or screening the identifiable personal

information of patients, service users or any other person?

☒ Yes ☐ No

Please give details below:

Clinical teams at the Royal Brompton Hospital will identify potential participants by reviewing the personal information of patients attending outpatients or inpatients on the ward. The clinical team will check whether participants meet the inclusion criteria and will make the initial approach to patients by providing them with an information sheet about the study.

A27-4. Will researchers or individuals other than the direct care team have access to identifiable personal information of any potential participants?

☐ Yes ☒ No

A28. Will any participants be recruited by publicity through posters, leaflets, adverts or websites?

☐ Yes ☒ No

A29. How and by whom will potential participants first be approached?

Potential participants: Patients and Informal Caregivers

The patients existing clinical team will approach potential patients and informal caregivers. Information sheets will be provided to all clinicians to distribute to potential participants. (appendix 6) At this time, if it is agreeable to the patient and they express a potential wish to participate in the research, the patient will be approached by a member of the research team. Therefore, before this study begins to recruit participants an educational programme will ensue to ensure all clinical teams are fully aware of the study aims, methods and inclusion and exclusion criteria. Therefore no potential research subject will be approached by the research team unless they are deemed appropriate by the clinical team and have received written and verbal information from them. Potential participants where possible will be given 24 hours to consider the study before the research team approach them to further discuss it. For those potential participants who are outpatients or are being discharged from hospital that day, consent may be obtained that day or the clinical team will obtain verbal consent for them to be contacted by telephone by the research team at a time convenient to them.

Potential Participants: Community Health Care Professionals

The community health care professionals present at the case conference or identified by the patient and informal caregiver will be sent an invitation letter by the research team through the post. This will explain what the study involves for their patient. Information sheet (appendix 12) and consent form for qualitative interview (appendix 13).

A30-1. Will you obtain informed consent from or on behalf of research participants?

☒ Yes ☐ No

If you will be obtaining consent from adult participants, please give details of who will take consent and how it will be done, with details of any steps to provide information (a written information sheet, video, or interactive material). Arrangements for adults unable to consent for themselves should be described separately in Part B Section 6, and for children in Part B Section 7.

If you plan to seek informed consent from vulnerable groups, say how you will ensure that consent is voluntary and fully informed.

Consent will be obtained from all participants. The patient and informal caregiver will be provided with an information sheet which they will be able to keep for reference (appendix 6). The researcher will explain the research and answer any questions the participant may have. All researchers have had training in assessing capacity and understand the ethical principles underpinning informed consent. A consent form will be completed (appendix 7). A copy of the consent form will be kept in the patient's notes and a copy will be kept in the study file. This is a longitudinal study and therefore at each contact the validity of the initial consent from participants will be reconfirmed.

If you are not obtaining consent, please explain why not.

Please enclose a copy of the information sheet(s) and consent form(s).

A30-2. Will you record informed consent (or advice from consultees) in writing?

☒ Yes ☐ No

A31. How long will you allow potential participants to decide whether or not to take part?

Participants where possible will be allowed a minimum of 24 hrs to decide whether they want to participate in the study. Instances in which this allowance of time may not be possible include if the patient is being seen in out-patients or the patient is due to be discharged from hospital that day. In all instances, it will be made clear to the patient and informal caregiver that if they choose to withdraw from the study at any point, their care will not be affected.

A33-1. What arrangements have been made for persons who might not adequately understand verbal explanations or written information given in English, or who have special communication needs? (e.g. translation, use of interpreters)

The case conference model currently only occurs in English, and therefore considering this and the additional costs involved with the use of translators and translation services for the documents, we will only be seeking English speaking patients.

A35. What steps would you take if a participant, who has given informed consent, loses capacity to consent during the study? *Tick one option only.*

- ☐ The participant and all identifiable data or tissue collected would be withdrawn from the study. Data or tissue which is not identifiable to the research team may be retained.
- ☒ The participant would be withdrawn from the study. Identifiable data or tissue already collected with consent would be retained and used in the study. No further data or tissue would be collected or any other research procedures carried out on or in relation to the participant.
- ☐ The participant would continue to be included in the study.
- ☐ Not applicable – informed consent will not be sought from any participants in this research.
- ☐ Not applicable – it is not practicable for the research team to monitor capacity and continued capacity will be assumed.

Further details:

Any patient or informal carer participant who loses capacity during the study will not be subject to any further interviews and will be withdrawn from the study. However, data already collected from the participant will be retained and used in the research. The information sheet makes participants aware that in the event of a loss of capacity, the research team would retain personal data collected and continue to use it confidentially for the purposes of this research study alone. If any participant becomes too unwell and unable to complete assessment, loses capacity or dies, they will be removed from the study. However, data already collected will be retained and used in analysis. If the intervention has been delivered and the patient has become too unwell to continue in the study, the informal caregiver's consent will be reconfirmed and data will continue to be collected from the informal caregiver alone until the patient dies. This issue is explicitly covered in the information sheet.

If you plan to retain and make further use of identifiable data/tissue following loss of capacity, you should inform participants about this when seeking their consent initially.

CONFIDENTIALITY

In this section, personal data means any data relating to a participant who could potentially be identified. It includes pseudonymised data capable of being linked to a participant through a unique code number.

Storage and use of personal data during the study

A36. Will you be undertaking any of the following activities at any stage (including in the identification of potential participants)? (Tick as appropriate)

- ☒ Access to medical records by those outside the direct healthcare team
- ☐ Electronic transfer by magnetic or optical media, email or computer networks
- ☐ Sharing of personal data with other organisations
- ☐ Export of personal data outside the EEA
- ☒ Use of personal addresses, postcodes, faxes, emails or telephone numbers
- ☒ Publication of direct quotations from respondents
- ☐ Publication of data that might allow identification of individuals
- ☒ Use of audio/visual recording devices
- ☒ Storage of personal data on any of the following:
- ☒ Manual files including X-rays
 - ☒ NHS computers
 - ☐ Home or other personal computers
 - ☐ University computers
 - ☐ Private company computers
 - ☐ Laptop computers

Further details:

Consent will be obtained for access to clinical records by research team. Identity of participants will be protected at all times by the use of encryption and using non-identifiable codes. Codes will be kept separately.

It states in the patient information sheet that medical records may be looked at by a member of the research team or regulatory authority. However the participants name will not be disclosed outside the hospital and they will not be identified in any report or publication that arises as a result of the study.

Storage of patient data will comply with legal requirements of the Data Protection Act.

A38. How will you ensure the confidentiality of personal data? Please provide a general statement of the policy and procedures for ensuring confidentiality, e.g. anonymisation or pseudonymisation of data.

Patients will be allocated an individual site specific number for these purposes. The NHS code of confidentiality will be followed.

A40. Who will have access to participants' personal data during the study? Where access is by individuals outside the direct care team, please justify and say whether consent will be sought.

Members of the research team (investigators and people they supervise) and regulatory authorities will have access to the medical notes. Consent will be sought for this and no one without the appropriate professional qualification will have access to this data.

Storage of patient data will comply with legal requirements of the Data Protection Act

Storage and use of data after the end of the study

A43. How long will personal data be stored or accessed after the study has ended?

- ☐ Less than 3 months
- ☐ 3 – 6 months
- ☐ 6 – 12 months
- ☐ 12 months – 3 years
- ☒ Over 3 years

If longer than 12 months, please justify:

The paper records and computer database will be held for 5 years in the Palliative Care department at the Royal

Brompton Hospital. It is policy at the Royal Brompton Hospital that all documentation relating to research is kept for 5 years

INCENTIVES AND PAYMENTS

A46. Will research participants receive any payments, reimbursement of expenses or any other benefits or incentives for taking part in this research?

☐ Yes ☒ No

A47. Will individual researchers receive any personal payment over and above normal salary, or any other benefits or incentives, for taking part in this research?

☐ Yes ☒ No

A48. Does the Chief Investigator or any other investigator/collaborator have any direct personal involvement (e.g. financial, share holding, personal relationship etc.) in the organisations sponsoring or funding the research that may give rise to a possible conflict of interest?

☐ Yes ☒ No

NOTIFICATION OF OTHER PROFESSIONALS

A49-1. Will you inform the participants' General Practitioners (and/or any other health or care professional responsible for their care) that they are taking part in the study?

☒ Yes ☐ No

If Yes, please enclose a copy of the information sheet/letter for the GP/health professional with a version number and date.

A49-2. Will you seek permission from the research participants to inform their GP or other health/care professional?

☒ Yes ☐ No

It should be made clear in the participant's information sheet if the GP/health professional will be informed.

PUBLICATION AND DISSEMINATION

A50. Will the research be registered on a public database?

☒ Yes ☐ No

Please give details, or justify if not registering the research.

The project will be registered on both the Royal Marsden and Royal Brompton trial databases.

A51. How do you intend to report and disseminate the results of the study? Tick as appropriate:

- ☒ Peer reviewed scientific journals
- ☒ Internal report
- ☒ Conference presentation
- ☐ Publication on website
- ☐ Other publication

- ☐ Submission to regulatory authorities
- ☐ Access to raw data and right to publish freely by all investigators in study or by Independent Steering Committee on behalf of all investigators
- ☐ No plans to report or disseminate the results
- ☒ Other (please specify)

The participation information sheet offers participants a copy of the research findings.
The participants can then indicate on the consent form if they would like to be informed on the results of the study.
Therefore, for those who wish to receive a copy a summary sheet of the findings will be sent to them through the post.
Relevant patient groups e.g the ILD patient group will be fed back to directly.

A53. Will you inform participants of the results?

☒ Yes ☐ No

Please give details of how you will inform participants or justify if not doing so.
Any patient, informal caregiver and health professional involved in the study will be offered a copy of the study results, and these will also be accessible to other patient groups within the Royal Brompton Hospital and Royal Marsden Hospitals. Relevant patient groups e.g the ILD patient group will be fed back to directly.

5. Scientific and Statistical Review

A54. How has the scientific quality of the research been assessed? Tick as appropriate:

- ☒ Independent external review
- ☐ Review within a company
- ☒ Review within a multi-centre research group
- ☒ Review within the Chief Investigator's institution or host organisation
- ☒ Review within the research team
- ☐ Review by educational supervisor
- ☐ Other

Justify and describe the review process and outcome. If the review has been undertaken but not seen by the researcher, give details of the body which has undertaken the review:
The scientific quality of the research has been reviewed by the Project Advisory Group which consists of multi-centre academics and health professionals:

Prof Irene Higginson- Professor King's College
Prof Athol Wells- Consultant and Head of Interstitial Lung Disease Unit Royal Brompton Hospital, Professor- National Heart and Lung Institute, Imperial College
Dr Joy Ross- Consultant Palliative Medicine and Senior Lecturer Imperial College
Dr Surinder Biring- Consultant Respiratory Medicine and Senior Lecturer King's College

In addition, the protocol was submitted to Marie Curie for an application for funding. Unfortunately we were not successful in this funding application. However, we received overall positive peer review comments (appendix 9) which we answered (appendix 10).

For all studies except non-doctoral student research, please enclose a copy of any available scientific critique reports, together with any related correspondence.

For non-doctoral student research, please enclose a copy of the assessment from your educational supervisor/institution.

A56. How have the statistical aspects of the research been reviewed? Tick as appropriate:

- ☐ Review by independent statistician commissioned by funder or sponsor
- ☐ Other review by independent statistician
- ☒ Review by company statistician

- ☒ Review by a statistician within the Chief Investigator's institution
- ☒ Review by a statistician within the research team or multi-centre group
- ☒ Review by educational supervisor
- ☐ Other review by individual with relevant statistical expertise
- ☐ No review necessary as only frequencies and associations will be assessed – details of statistical input not required

In all cases please give details below of the individual responsible for reviewing the statistical aspects. If advice has been provided in confidence, give details of the department and institution concerned.

	Title Forename/Initials Surname
	Kabir Mohammed
Department	Department of Statistics
Institution	The Royal Marsden NHS Foundation Trust
Work Address	Downs Rd
	Sutton
Post Code	SM2 5PT
Telephone	
Fax	
Mobile	
E-mail	kabir.mohammed@rmh.nhs.uk

Please enclose a copy of any available comments or reports from a statistician.

A57. What is the primary outcome measure for the study?

The primary outcome will be to compare the change in POS scores recorded at week 4 and baseline for each group; POS scores evaluate symptoms and palliative concerns using the Palliative Care Outcome Scale (POS)(20)(appendix 11). This comprises eight questions on anxiety, patient and informal caregiver concerns, and practical needs, each rated 0-4. This scoring system will ensure that there is some ongoing data available if the patient becomes unwell and is no longer able to complete the study.

A58. What are the secondary outcome measures? (if any)

Secondary outcomes will include comparison of the patient and informal caregiver POS in this study to see how interchangeable/reliable the 2 assessments are. The other secondary outcomes will focus on quality of life. (appendix 3) At each interview, service use questions will be asked which will record the frequency and types of health/social services received (see appendix 4, 12 & 13) in order that an accurate evaluation of cost of care per patient can be made. In addition semi-structured qualitative interviews will be conducted with patients, informal caregivers and health professionals. Prompts will include views of the case conference, the guidelines and what level of input was needed after the case conference. A record will be made of when and where the patient dies.

A59. What is the sample size for the research? How many participants/samples/data records do you plan to study in total? If there is more than one group, please give further details below.

Total UK sample size: 52
Total international sample size (including UK):
Total in European Economic Area:

Further details:

We anticipate recruiting 26 patients per group ie 52 in all. Based on the local patient numbers, we estimate to identify 2 patients per week, and recruit and retain at least 1 each week giving 52 patients in one year. We anticipate that this number is sufficient to estimate the change in POS score between baseline and 4 weeks with reasonable precision.

(Assuming a standard deviation of 2, a 95% confidence interval for the difference between the intervention and usual care group would be 2.2 units wide ie mean difference \pm 1.1 units, which we judge to be sufficiently precise). The POS data are likely to be skew and the study will allow time to identify the most appropriate way to analyse these data for a later phase 3 study.

As part of this study we will check the validity and reliability of the modifications to POS.

There will initially be 15 patients for the qualitative work (5 patients, 5 informal caregivers and 5 health professionals). These interviews will be analysed and if there are ongoing new themes emerging then further interviews will be conducted until there are no new themes emerging.

A60. How was the sample size decided upon? *If a formal sample size calculation was used, indicate how this was done, giving sufficient information to justify and reproduce the calculation.*

We anticipate recruiting 26 patients per group ie 52 in all. Based on the local patient numbers, we estimate to identify 2 patients per week, and recruit and retain at least 1 each week giving 52 patients in one year. We anticipate that this number is sufficient to estimate the change in POS score between baseline and 4 weeks with reasonable precision. (Assuming a standard deviation of 2, a 95% confidence interval for the difference between the intervention and usual care group would be 2.2 units wide ie mean difference \pm 1.1 units, which we judge to be sufficiently precise). The POS data are likely to be skew and the study will allow time to identify the most appropriate way to analyse these data for a later phase 3 study.

A61. Will participants be allocated to groups at random?

☒ Yes ☐ No

If yes, please give details of the intended method of randomisation:

After providing consent and baseline interview, patients at RBH site meeting inclusion criteria will be allocated to fast track or waiting list by independent off-site randomisation. Randomisation will be provided by The Institute of Cancer Research - Clinical Trials and Statistics Unit (ICR-CTSU). The ICR-CTSU will provide a unique randomisation number (Trial ID) for each patient together with the allocated treatment code. Treatment allocation (fast track/waiting list group) will be by computer generated random permuted blocks.

A62. Please describe the methods of analysis (statistical or other appropriate methods, e.g. for qualitative research) by which the data will be evaluated to meet the study objectives.

The change in POS score (Baseline to 4 Week) will be compared between groups. Unpaired t-test will be used to compare POS symptom scores between the fast-track and waiting list group at both 4 weeks (before the waiting list group receives the intervention) and 8 weeks. If assumptions of normality are not met the data will be log transformed or use non-parametric method of analysis. Summary of POS scores of all patients in each group will be reported at each time point.

We will also perform secondary analyses using analysis of covariance (ANCOVA) to examine group differences in 4 and 8 week POS values adjusted for baseline values. We shall examine trends in POS values across time as a longitudinal analysis using a linear mixed model. The profile of the POS scores over the time points will be modeled together with a modeling of the occurrence of (possibly informative) missing values. The analysis will adjust for baseline POS and include age, gender and degree of disease as candidate predictive variables.

Using Bland-Altman graphical and overall agreement calculation method, patients' and caregiver' POS scores will be compared. The overall agreement and its 95% confidence interval will be reported.

Data on resource use will be combined with unit cost data to provide estimate of overall costs per participant in each group. Following Gomes et al suggestion, cost will be assessed using a broad perspective - including costs to health, social, and voluntary services and informal caregivers. Data regarding the use of health and social services will be collected at each interview. These will take into account salaries, overheads, training and the ratio of direct patient contact time to non-contact time.

The qualitative interviews will be audio-recorded, transcribed verbatim, and entered into NVivo 9.0. The interview data will be initially analysed for themes by hand using the constant comparative approach, and then cross-checked and refined using NVivo. Data will be initially coded as 'free nodes', and these will then be grouped into broader themes. Dual coding will be conducted and cross checked for accuracy. The framework approach will be used to analyse the

qualitative data.

6. MANAGEMENT OF THE RESEARCH

A63. Other key investigators/collaborators. Please include all grant co-applicants, protocol co-authors and other key members of the Chief Investigator's team, including non-doctoral student researchers.

	Title	Forename/Initials	Surname
	Dr	Sabrina	Bajwah
Post	Clinical Research Fellow		
Qualifications	MBChB, MRCP, MSc		
Employer	Royal Marsden NHS foundation Trust		
Work Address	Department of Palliative Medicine		
	Royal Marsden Hospital		
	Fulham Rd		
Post Code	SW3 6JJ		
Telephone	02078082761		
Fax	02078 118132		
Mobile			
Work Email	sabrina.bajwah@kcl.ac.uk		

	Title	Forename/Initials	Surname
	Professor	Irene J	Higginson
Post	Head of Palliative Care, Policy and Rehabilitation Department, King's College London		
Qualifications	BMedSci BMBS PhD FFPHM FRCP		
Employer	King's College London		
Work Address	Cicely Saunders Institute		
	Bessemer Rd		
	Denmark Hill		
Post Code	SE5 9RJ		
Telephone	02078 485516		
Fax	02078 485517		
Mobile			
Work Email	irene.higginson@kcl.ac.uk		

	Title	Forename/Initials	Surname
	Dr	Joy R	Ross
Post	Palliative Medicine Consultant		
Qualifications	MB.BS BSc PhD MRCP		
Employer	Royal Marsden NHS Foundation Trust		
Work Address	Department of Palliative Medicine		
	Royal Marsden Hospital		
	Fulham Rd		
Post Code	SW3 6JJ		
Telephone	02078082761		
Fax	02078 118132		
Mobile			
Work Email	julia.riley@rmh.nhs.uk		

	Title	Forename/Initials	Surname
	Professor	Athol U	Wells
Post			
Qualifications	MBChB FRACP MD FRCP FRCR		
Employer	Royal Brompton Hospital Foundation NHS Trust		
Work Address	Interstitial Lung Disease Unit, Emmanuel KAYe Building, Manresa Rd Chelsea		
Post Code	SW3 6LR		
Telephone	02073518327		
Fax			
Mobile			
Work Email	athol.wells@rbht.nhs.uk		
	Title	Forename/Initials	Surname
	Dr	Surinder S	Biring
Post	Consultant in Respiratory Medicine		
Qualifications	BSc MBChB MRCP MD		
Employer	King's College NHS Foundation Trust		
Work Address	Department of Respiratory Medicine King's College Hospital Denmark Hill		
Post Code	SE5 9RS		
Telephone	02032994630		
Fax	02032993791		
Mobile			
Work Email	surinder.biring@nhs.net		
	Title	Forename/Initials	Surname
	Dr	Jonathan	Koffman
Post	Senior Lecturer, King's College London		
Qualifications	PhD		
Employer	King's College London		
Work Address	Cicely Saunders Institute Bessemer Rd Denmark Hill		
Post Code	SE5 9RJ		
Telephone	02078485516		
Fax	02078485517		
Mobile			
Work Email	jonathan.koffman@kcl.ac.uk		
	Title	Forename/Initials	Surname
		Kabir	Mohammed
Post	Statistician		
Qualifications	Department of Statistics		
Employer	The Royal Marsden NHS Foundation Trust		

Work Address	Downs Rd
	Sutton
Post Code	SM2 5PT
Telephone	
Fax	
Mobile	
Work Email	kabir.mohammed@rmh.nhs.uk

A64. Details of research sponsor(s)

A64-1. Sponsor

Lead Sponsor

Status: ☒ NHS or HSC care organisation

Commercial status:

☐ Academic☐ Pharmaceutical industry☐ Medical device industry☐ Local Authority☐ Other social care provider (including voluntary sector or private organisation)☐ Other*If Other, please specify:*

Contact person

Name of organisation Royal Marsden NHS Foundation Trust

Given name Jane

Family name Lawrence

Address Royal Marsden Hospital

Town/city Downs Rd

Post code SM2 5PT

Country UNITED KINGDOM

Telephone

Fax

E-mail jane.lawrence@rmh.nhs.uk

Is the sponsor based outside the UK?

☐ Yes ☒ No*Under the Research Governance Framework for Health and Social Care, a sponsor outside the UK must appoint a legal representative established in the UK. Please consult the guidance notes.*

A65. Has external funding for the research been secured?

☒ Funding secured from one or more funders☐ External funding application to one or more funders in progress☐ No application for external funding will be made

Please give details of funding applications.

Organisation Marie Curie Cancer Care
Address 89 Albert Embankment

Post Code SE1 7TP
Telephone 0845 634 2555

Fax

Mobile

Email jackie.stokes@mariecurie.org.uk

Funding Application Status: ☒ Secured ☐ In progress

Amount: 2 years pay

Duration

Years: 2

Months:

If applicable, please specify the programme/funding stream:

What is the funding stream/programme for this research project?

The H2H nurse is funded by Marie Curie for a duration of 2 years. The remainder of the project (including the salary of the research fellow) is being funded by the Royal Marsden and Royal Brompton Palliative Care budget. This will be ongoing till the project is completed.

What type of research project is this?

- ☒ Standalone project
☐ Project that is part of a programme grant
☐ Project that is part of a fellowship/personal award/research training award
☐ Other

Other – please state:

A67. Has this or a similar application been previously rejected by a Research Ethics Committee in the UK or another country?

☐ Yes ☒ No

Please provide a copy of the unfavourable opinion letter(s). You should explain in your answer to question A6-2 how the reasons for the unfavourable opinion have been addressed in this application.

A68. Give details of the lead NHS R&D contact for this research:

Title Forename/Initials Surname
Ms Jane Lawrence
Organisation Royal Marsden NHS Foundation Trust
Address Royal Marsden Hospital
Downs Rd

Sutton
 Post Code SM2 5PT
 Work Email jane.lawrence@mh.nhs.uk
 Telephone 020866 13909
 Fax
 Mobile

Details can be obtained from the NHS R&D Forum website: <http://www.r4forum.nhs.uk>

A69-1. How long do you expect the study to last in the UK?

Planned start date: 01/08/2011

Planned end date: 01/11/2012

Total duration:

Years: 1 Months: 3 Days: 0

A71-1. Is this study?

- ☐ Single centre
☒ Multicentre

A71-2. Where will the research take place? (Tick as appropriate)

- ☒ England
☐ Scotland
☐ Wales
☐ Northern Ireland
☐ Other countries in European Economic Area

Total UK sites in study 2

Does this trial involve countries outside the EU?

- ☐ Yes ☒ No

A72. What host organisations (NHS or other) in the UK will be responsible for the research sites? Please indicate the type of organisation by ticking the box and give approximate numbers of planned research sites:

- ☒ NHS organisations in England 2
☐ NHS organisations in Wales
☐ NHS organisations in Scotland
☐ HSC organisations in Northern Ireland
☐ GP practices in England
☐ GP practices in Wales
☐ GP practices in Scotland
☐ GP practices in Northern Ireland
☐ Social care organisations
☐ Phase 1 trial units
☐ Prison establishments
☐ Probation areas
☐ Independent hospitals

- ☐ Educational establishments
☐ Independent research units
☐ Other (give details)

Total UK sites in study: 2

A76. Insurance/indemnity to meet potential legal liabilities

Note: in this question to NHS indemnity schemes include equivalent schemes provided by Health and Social Care (HSC) in Northern Ireland

A76-1. What arrangements will be made for insurance and/or indemnity to meet the potential legal liability of the sponsor(s) for harm to participants arising from the management of the research? Please tick box(es) as applicable.

Note: Where a NHS organisation has agreed to act as sponsor or co-sponsor, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For all other sponsors, please describe the arrangements and provide evidence.

- ☒ NHS indemnity scheme will apply (NHS sponsors only)
☐ Other insurance or indemnity arrangements will apply (give details below)

Please enclose a copy of relevant documents.

A76-2. What arrangements will be made for insurance and/or indemnity to meet the potential legal liability of the sponsor(s) or employer(s) for harm to participants arising from the design of the research? Please tick box(es) as applicable.

Note: Where researchers with substantive NHS employment contracts have designed the research, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For other protocol authors (e.g. company employees, university members), please describe the arrangements and provide evidence.

- ☒ NHS indemnity scheme will apply (protocol authors with NHS contracts only)
☐ Other insurance or indemnity arrangements will apply (give details below)

Please enclose a copy of relevant documents.

A76-3. What arrangements will be made for insurance and/or indemnity to meet the potential legal liability of investigators/collaborators arising from harm to participants in the conduct of the research?

Note: Where the participants are NHS patients, indemnity is provided through the NHS schemes or through professional indemnity. Indicate if this applies to the whole study (there is no need to provide documentary evidence). Where non-NHS sites are to be included in the research, including private practices, please describe the arrangements which will be made at these sites and provide evidence.

- ☒ NHS indemnity scheme or professional indemnity will apply (participants recruited at NHS sites only)
☐ Research includes non-NHS sites (give details of insurance/indemnity arrangements for these sites below)

Please enclose a copy of relevant documents.

PART C: Overview of research sites

Please enter details of the host organisations (Local Authority, NHS or other) in the UK that will be responsible for the research sites. For NHS sites, the host organisation is the Trust or Health Board. Where the research site is a primary care site, e.g. GP practice, please insert the host organisation (PCT or Health Board) in the Institution row and insert the research site (e.g. GP practice) in the Department row.

Research site		Investigator/ Collaborator/ Contact	
Institution name	Royal Marsden Hospital	Title	Dr
Department name	Palliative Care Department	First name/	Julia
Street address	Chelsea	Initials	
Town/city		Surname	Riley
Post Code	SW3 6JJ		
Institution name	Royal Brompton Hospital	Title	Dr
Department name	Interstitial Lung Disease Unit	First name/	Julia
Street address	Sydney Street	Initials	
Town/city	London	Surname	Riley
Post Code	SW3 6NP		

PART D: Declarations**D1. Declaration by Chief Investigator**

1. The information in this form is accurate to the best of my knowledge and belief and I take full responsibility for it.
2. I undertake to abide by the ethical principles underlying the Declaration of Helsinki and good practice guidelines on the proper conduct of research.
3. If the research is approved I undertake to adhere to the study protocol, the terms of the full application as approved and any conditions set out by review bodies in giving approval.
4. I undertake to notify review bodies of substantial amendments to the protocol or the terms of the approved application, and to seek a favourable opinion from the main REC before implementing the amendment.
5. I undertake to submit annual progress reports setting out the progress of the research, as required by review bodies.
6. I am aware of my responsibility to be up to date and comply with the requirements of the law and relevant guidelines relating to security and confidentiality of patient or other personal data, including the need to register when necessary with the appropriate Data Protection Officer. I understand that I am not permitted to disclose identifiable data to third parties unless the disclosure has the consent of the data subject or, in the case of patient data in England and Wales, the disclosure is covered by the terms of an approval under Section 251 of the NHS Act 2006.
7. I understand that research records/data may be subject to inspection by review bodies for audit purposes if required.
8. I understand that any personal data in this application will be held by review bodies and their operational managers and that this will be managed according to the principles established in the Data Protection Act 1998.
9. I understand that the information contained in this application, any supporting documentation and all correspondence with review bodies or their operational managers relating to the application:
 - Will be held by the main REC or the GTAC (as applicable) until at least 3 years after the end of the study; and by NHS R&D offices (where the research requires NHS management permission) in accordance with the NHS Code of Practice on Records Management.
 - May be disclosed to the operational managers of review bodies, or the appointing authority for the main REC, in order to check that the application has been processed correctly or to investigate any complaint.
 - May be seen by auditors appointed to undertake accreditation of RECs.
 - Will be subject to the provisions of the Freedom of Information Acts and may be disclosed in response to requests made under the Acts except where statutory exemptions apply.
10. I understand that information relating to this research, including the contact details on this application, may be held on national research information systems, and that this will be managed according to the principles established in the Data Protection Act 1998.
11. I understand that the summary of this study will be published on the website of the National Research Ethics Service (NRES), together with the contact point for enquiries named below. Publication will take place no earlier than 3 months after issue of the ethics committee's final opinion or the withdrawal of the application.

Contact point for publication (Not applicable for R&D Forms)

NRES would like to include a contact point with the published summary of the study for those wishing to seek further information. We would be grateful if you would indicate one of the contact points below.

☒ Chief Investigator

☐ Sponsor

☐ Study co-ordinator

- ☐ Student
☐ Other – please give details
☐ None

Access to application for training purposes (*Not applicable for R&D Forms*)

Optional – please tick as appropriate:

☒ I would be content for members of other RECs to have access to the information in the application in confidence for training purposes. All personal identifiers and references to sponsors, funders and research units would be removed.

Signature:

Print Name: Dr Julia Riley

Date: 09/06/2011 (d/d/m/yyyy)

D2. Declaration by the sponsor's representative

If there is more than one sponsor, this declaration should be signed on behalf of the co-sponsors by a representative of the lead sponsor named at A64-1.

I confirm that:

1. This research proposal has been discussed with the Chief Investigator and agreement in principle to sponsor the research is in place.
2. An appropriate process of scientific critique has demonstrated that this research proposal is worthwhile and of high scientific quality.
3. Any necessary indemnity or insurance arrangements, as described in question A76, will be in place before this research starts. Insurance or indemnity policies will be renewed for the duration of the study where necessary.
4. Arrangements will be in place before the study starts for the research team to access resources and support to deliver the research as proposed.
5. Arrangements to allocate responsibilities for the management, monitoring and reporting of the research will be in place before the research starts.
6. The duties of sponsors set out in the Research Governance Framework for Health and Social Care will be undertaken in relation to this research.
7. I understand that the summary of this study will be published on the website of the National Research Ethics Service (NRES), together with the contact point for enquiries named in this application. Publication will take place no earlier than 3 months after issue of the ethics committee's final opinion or the withdrawal of the application.

Signature:

Print Name: Jane Lawrence

Post: Head of Research Governance and Development

Organisation: Royal Marsden NHS Foundation Trust

Date: 10/06/2011 (dd/mm/yyyy)

D3. Declaration for student projects by academic supervisor(s)

1. I have read and approved both the research proposal and this application. I am satisfied that the scientific content of the research is satisfactory for an educational qualification at this level.
2. I undertake to fulfil the responsibilities of the supervisor for this study as set out in the Research Governance Framework for Health and Social Care.
3. I take responsibility for ensuring that this study is conducted in accordance with the ethical principles underlying the Declaration of Helsinki and good practice guidelines on the proper conduct of research, in conjunction with clinical supervisors as appropriate.
4. I take responsibility for ensuring that the applicant is up to date and complies with the requirements of the law and relevant guidelines relating to security and confidentiality of patient and other personal data, in conjunction with clinical supervisors as appropriate.

Academic supervisor 1

Signature:

Print Name: Prof Irene J Higginson

Post: Professor and Head of Department of Palliative Care, Policy and Rehabilitation

Organisation: King's College London

Date: 13/06/2011 (dd/mm/yyyy)

Academic supervisor 2

Signature:

Print Name: Dr Julia Riley

Post: Head of Palliative Care department

Organisation: Royal Marsden and Royal Brompton NHS Foundation Trusts

Date: 09/06/2011 (dd/mm/yyyy)

Academic supervisor 3

Signature:

Print Name: Athol U Wells

Post: Professor and Head of Interstitial Lung Disease Unit

Organisation: Royal Brompton Hospital & National Heart and Lung Institute, Imperial College London

Date: 09/06/2011 (dd/mm/yyyy)

Academic supervisor 4

Signature:
Print Name:	Jonathan Koffman
Post:	Senior Lecturer
Organisation:	King's College London
Date:	14/06/2011 (dd/mm/yyyy)

NRES Committee London - Chelsea

Room 4W/12, 4th Floor West
Charing Cross Hospital
Fulham Palace Road
London W6 8RF

Telephone: 020 331 17251

Facsimile:

16 August 2011

Dr Julia Riley
Consultant and Head of Palliative Care Department
Royal Marsden Hospital NHS Trust
Department of Palliative Medicine
Royal Marsden Hospital
Fulham Rd
SW3 6JJ

Dear Dr Riley

Study title: A fast track randomised controlled trial to evaluate a
Hospital2Home palliative care service for patients with advanced
Progressive Idiopathic Fibrotic Interstitial Lung Disease
REC reference: 11/LO/0999

Thank you for your letter of 28 July 2011, responding to the Committee's request for further information on the above research and submitting revised documentation.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Non-NHS sites

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at <http://www.rdforum.nhs.uk>.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

<i>Document</i>	<i>Version</i>	<i>Date</i>
Covering Letter		08 June 2011
GP/Consultant Information Sheets	1.0	27 February 2011
Interview Schedules/Topic Guides	1.0	27 February 2011
Investigator CV	Dr Riley	
Other: Prof Irene Higginson	cv	
Other: Prof Athol Wells	cv	
Other: Dr Sabrina Bajwah	cv	
Other: Dr Jonathan Koffman	cv	
Other: Table showing admissions to RBH 2009		
Other: Figure of study design		
Other: Care plan for H2H case conference	1.0	27 February 2011
Other: Case conference form	1.0	27 February 2011
Other: Post case Conference follow up form	1.0	27 February 2011
Other: Hospital2Home patient list instructions for On Call staff	1.0	27 February 2011
Other: Preferred priorities of care document	1.0	27 February 2011
Other: Outcome measures	1.2	26 May 2011
Other: Adapted POS	1.0	27 February 2011
Other: AUW prognostic tool		
Participant Consent Form: Carer	1.1	23 March 2011
Participant Consent Form: Healthcare Professional	1.1	25 March 2011
Participant Consent Form: Patient	1.2	02 June 2011
Participant Information Sheet: Healthcare Professional	1.0	27 February 2011
Participant Information Sheet: Patient	1.3	28 July 2011
Participant Information Sheet: Carer	1.1	28 July 2011

Protocol	1.4	08 June 2011
REC application	74961/221536/1/651	14 June 2011
Referees or other scientific critique report	Marie Curie Peer Review Comments	
Response to Request for Further Information		28 July 2011
Summary/Synopsis	Figure of Study	

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document "*After ethical review – guidance for researchers*" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

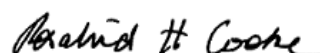
You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

11/LO/0999	Please quote this number on all correspondence
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With the Committee's best wishes for the success of this project

Yours sincerely



Pp Ms Tricia Pank
Vice Chair

Email: Rosalind.cooke@imperial.nhs.uk

Enclosures: "After ethical review – guidance for researchers" [\[SL-AR2\]](#)
Copy to: Miss Jane Lawrence

Dr Julia Riley
Consultant and Head of Palliative Care Department
Royal Brompton and Harefield NHS Foundation Trust
Sydney Street
London SW3 6NP

Tuesday 04th October 2011

Dear Dr Riley,

A fast-track randomised controlled trial to evaluate a Hospital 2 Home (H2H) palliative care service for patients with advanced progressive idiopathic fibrotic lung disease.

Project Reference: 2011OE007B
R&D Form Submission Code: 74961/248548/14/917
SSIF Submission Code: 74961/249284/6/680/96559/223323

Thank you for registering your Research Project with the R&D office. The project details have been entered on our Research Management Database. Please ensure you keep the R&D office informed of the following:

- changes to the status of the project e.g. abandoned, completed etc
- changes to the funding arrangements
- changes to the original application e.g. change in personnel or amendments requiring ethical review

RESEARCH GOVERNANCE

Royal Brompton & Harefield NHS Foundation Trust manages all research in accordance with the requirements of the research governance framework. Whilst working as an employee of the Royal Brompton and Harefield NHS Foundation Trust, or holding an Honorary Contract to do research which involves NHS staff or patients, their organs tissue or data, you must comply with all reporting requirements, systems, and duties of action put in place by the Trust to deliver research governance. As such if you are acting as either Chief/Principal Investigator your responsibilities under this framework include:

- ensuring compliance with protocol and advising of any changes to the protocol
- reporting any adverse events whether related to research or not to clinical governance/ethics/R&D
- taking appropriate urgent safety measures
- ensuring adherence to the principles of ICH GCP
- ensuring researchers have necessary expertise
- ensuring compliance with the Data Protection Act
- ensure adequate monitoring arrangements are in place
- ensure compliance with the Human Tissue Act

The Trust routinely audits a minimum of 10% of its research activity. This is to ensure that research is progressing satisfactorily and to guard against research fraud. You are requested to maintain and retain appropriate records of your research, and assist the Trust as and when required should any such audit take place in your area.

CLINICAL TRIALS REGISTRATION

The majority of research journals will now only publish research that has been registered at a publicly accessible database before the enrolment of the first patient. Where research projects are sponsored by either the Trust or Imperial College it is recommended that the project is registered at www.ClinicalTrials.gov which is free of charge. For Trust sponsored projects please contact 020 7351 8574 and an account will be set-up for you to register your project. Similarly, please contact clinical.researchoffice@imperial.ac.uk for an account to register Imperial College sponsored projects.

In receiving this letter you are agreeing to abide by the terms as outlined above. Please accept this letter as the Trust's authorisation to commence your research.

Please note that in the interim we will be discussing with the R&D department at RMH regarding the Trust receiving appropriate recognition of accruals for this study.

Yours sincerely



Wendy Butcher
Head of Research Governance and Performance

Appendix 1**Notification of Amendment Cover Sheet**

Please complete this form when you submit all documents relating to your amendment to the R&D Office.

Part A – Where to Send your Request

To: R&D Office
Royal Marsden NHS Foundation Trust
Tel: 0208 661 3909
Fax: 0208 915 6700
Email: research.development@rmh.nhs.uk

R&D Office use only

Date received:

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Amendment R&D Ref:

Part B – Your Details

From: Jenna Frizell
Senior Trials Coordinator, Palliative Care and Pain, Fulham Road
Tel: 4648
Fax: 02078118307
Email: Jenna.frizell@rmh.nhs.uk

Part C – Sponsor Details

(please tick)
RMH-sponsored ☒
RMH-hosted (please specify below) ☐

Part D – Study Details

A fast-track randomised controlled trial to evaluate a Hospital2Home

Trial Name: palliative care service for patients with advanced Progressive Idiopathic
Fibrotic Interstitial Lung Disease

non-CTIMP

CCR reference number: CCR

3	6	6	9
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CSP reference number: n/a

Chief Investigator/ Dr Julia Riley

Principal Investigator: Dr Joy Ross, Dr Sabrina Bajwah

Part E – Notification to other Departments (If yes please tick)

Amendment impacts ARSAC	<input type="checkbox"/>
Amendment impacts Radiology	<input type="checkbox"/>
Amendment impacts Pharmacy	<input type="checkbox"/>
Amendment impacts Finance	<input type="checkbox"/>
Amendment impacts Contracts (Please see procedure below)	<input type="checkbox"/>

<u>Contract Amendments Procedure</u>			
	YES	NO	N/A
Amendment impacts Intellectual Property (e.g. involves new assays or translational PD studies)	<input type="checkbox"/>	<input type="checkbox"/>	X
Amendment impacts Financial Arrangements Appendix:			
Finance approval?	<input type="checkbox"/>	<input type="checkbox"/>	X
Pharmacy approval?	<input type="checkbox"/>	<input type="checkbox"/>	X
<ul style="list-style-type: none"> • Please ensure that an electronic copy of the contract (scan hard copies of contract) is sent to the Associate Contract Manager. • Please ensure that all required Finance and Pharmacy approvals are sent to the Associate Contract Manager as soon as they are received. 			

Part F – Amendment Details

If large sections of text / documents are to be changed and will not fit in the table below, please supply a summary of changes and indicate the number of supplemental pages below.

For Sponsored trials under 'CI Opinion' column, please indicate whether the amendment should be classed as:

1 – (Substantial amendment)

2 – (Non-substantial amendment)

Document(s) Version and Date		Details of amendment (include page numbers where appropriate)	Brief rationale to support application for amendment	CI Opinion (1 or 2)	R&D Opinion (1 or 2)
Current	Amended				
Patient CRF v1.3 20.10.11	Patient CRF v1.4 17.05.12	As part of the CRF, change from using the McGill to the St George's Respiratory Questionnaire	As a result of a systematic review that has been conducted, it has become apparent that the McGill Quality of Life Tool is not used in respiratory medicine and a more appropriate questionnaire to use instead would be the St George's Respiratory Questionnaire. It is envisaged that this will not have any implications for the safety or welfare of participants.	2	

Number of Supplemental Pages:


Copy of CRF 1.4
clean and CRF 1.3
tracked changes
attached.

PI, co-investigator

Dr Joy Ross

Date

17.05.12


17/5/12

Study Statistician Signature (RMH/ICR sponsored trials only)	
Date	

CCR Chairman/R&D Signature	
Date	

Prof David Dearnaley (Chairman)
David.dearnaley@icr.ac.uk

Research & Development Office
West Wing, Downs Road,
RMH Sutton

Tel: 020 8661 3047
Fax: 020 8915 6700

Committee for Clinical Research

Dr Julia Riley
Palliative Care
Royal Marsden NHS Trust
Fulham Road
Chelsea
London
SW3 6JJ

29 May 2012

Dr Julia Riley

ID: CCR3669

**A fast-track randomised controlled trial to evaluate a Hospital2Home
palliative care service for patients with advanced Progressive Idiopathic
Fibrotic Interstitial Lung Disease**

Thank you for your amendment received in R&D on 23.5.2012 with enclosures which provide details of the following non-substantial amendment to the above project.

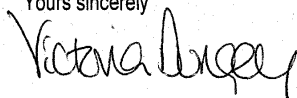
Amendment:
Patient CRF v1.4 dated 17.5.2012 - change from using the McGill to the St George's Respiratory
Questionnaire

R&D Amendment ID: AM1205/48

I am pleased to inform you that this amendment has been acknowledged and approved by the Deputy
Chair of the Committee for Clinical Research on 28.5.2012.

If the R&D Office can be of any further assistance, please do not hesitate to contact us.

Yours sincerely



Victoria Dungey

Clinical R&D Administrator

Copy to: Miss Jenna Frizell,

Appendix 1**Notification of Amendment Cover Sheet**

Please complete this form when you submit all documents relating to your amendment to the R&D Office.

Part A – Where to Send your Request

To: R&D Office
 Royal Marsden NHS Foundation Trust
 Tel: 0208 661 3909
 Fax: 0208 915 6700
 Email: research.development@rmh.nhs.uk

R&D Office use only

Date received:

--

Amendment R&D Ref:

Part B – Your Details

From: Jenna Frizell
 Senior Trials Coordinator, Palliative Care and Pain, Fulham Road
 Tel: 4648
 Fax: 02078118307
 Email: Jenna.frizell@rmh.nhs.uk

Part C – Sponsor Details

(please tick)

RMH-sponsored

X

RMH-hosted (please specify below)

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Part D – Study Details

A fast-track randomised controlled trial to evaluate a Hospital2Home

Trial Name: palliative care service for patients with advanced Progressive Idiopathic
 Fibrotic Interstitial Lung Disease

non-CTIMP

CCR reference number: CCR

3	6	6	9
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CSP reference number: n/a

Chief Investigator/ Dr Julia Riley

Principal Investigator: Dr Joy Ross, Dr Sabrina Bajwah

Part E – Notification to other Departments (if yes please tick)

Amendment impacts ARSAC	<input type="checkbox"/>
Amendment impacts Radiology	<input type="checkbox"/>
Amendment impacts Pharmacy	<input type="checkbox"/>
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Amendment impacts Contracts (Please see procedure below)	<input type="checkbox"/>

<u>Contract Amendments Procedure</u>			
	YES	NO	N/A
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Amendment impacts Financial Arrangements Appendix:			
Finance approval?	<input type="checkbox"/>	<input type="checkbox"/>	X
Pharmacy approval?	<input type="checkbox"/>	<input type="checkbox"/>	X
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Part F – Amendment Details

If large sections of text / documents are to be changed and will not fit in the table below, please supply a summary of changes and indicate the number of supplemental pages below.

For Sponsored trials under 'CI Opinion' column, please indicate whether the amendment should be classed as:

1 – (Substantial amendment)

2 – (Non-substantial amendment)

Document(s) Version and Date		Details of amendment (include page numbers where appropriate)	Brief rationale to support application for amendment	CI Opinion (1 or 2)	R&D Opinion (1 or 2)
Current	Amended				
Carer consent form v1.1	Carer consent form v1.2	P1&2 change of version number.	Change version number to reflect amendment.	2	
Carer information sheet v1.1	Carer information sheet v1.2	P1&2 changes of wording resulting from patient feedback, change in version number.	Please see cover letter for full details of amendment. Following feedback from patients and carers on the patient and carer information sheets, we have made the changes attached. Change in version number to reflect amendment.	1	
Patient consent form v1.2	Patient consent form v1.3	P1&2 change of version number.	Change version number to reflect amendment.	2	
Patient information sheet v1.3	Patient information sheet v1.4	P1, 2 & 3 changes of wording resulting from patient feedback, change in version number.	Please see cover letter for full details of amendment. Following feedback from patients and carers on the patient and carer information sheets, we have made the changes attached. Change in version number to reflect amendment. During the course of the trial, it has become apparent that it is extremely difficult to get the case conference for those patients who are randomised to the fast track group organised within one week and sometimes the waiting list groups' case conference at exactly 4 weeks. We would therefore like to be able to have some	1	
Protocol v1.4	Protocol v1.5	P7-10 changes to study design, outcome measures and endpoints. P12 extension to study end date.		1	

		<p>flexibility in the time points of the case conferences and the assessments to be able to capture the data pre and post case conference.</p> <p>Patients with PIF-ILD who fulfill the diagnostic criteria but do not necessarily rate as less than one year prognosis are being referred to the study. These patients have clear specialist palliative care needs. As recruitment has been slower than expected, we would like to recruit these patients. We would still be noting what these patients score on the prognostic scoring system.</p>	
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1. Carer consent form v1.1 and v1.2


2. Carer information sheet v1.1 and v1.2

3. Patient consent form v1.2 and v1.3

4. Patient information sheet v1.3 and v1.4

5. Protocol v1.4 and v1.5

Number of Supplemental Pages:

Co-investigator	Date
Dr Sabrina Bajwah	

Study Statistician Signature <i>(RMH/ICR sponsored trials only)</i>	n/a external statistician
Date	

CCR Chairman/R&D Signature	
Date	

NRES Committee London - Chelsea

HRA
Research Ethics Committee (REC) London Centre
Ground Floor
80 Skipton House
London Road
London, SE1 6LH

Tel: 020 7972 2536

14 November 2012

Dr Julia Riley
Consultant and Head of Palliative Care Department
Royal Marsden Hospital NHS Trust
Department of Palliative Medicine
Royal Marsden Hospital
Fulham Rd, SW3 6JJ

Dear Dr Riley

Study title: A fast track randomised controlled trial to evaluate a Hospital2Home palliative care service for patients with advanced Progressive Idiopathic Fibrotic Interstitial Lung Disease

REC reference: 11/LO/0999

Amendment number: 2 21.08.12

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Letter from Sponsor		31 August 2012
Participant Consent Form: Carer	1.2	01 August 2012
Participant Consent Form: Patient	1.3	01 August 2012
Participant Information Sheet: Carer	1.2	01 August 2012
Participant Information Sheet: Patient	1.4	01 August 2012
Protocol	1.5	08 August 2012
Notice of Substantial Amendment (non-CTIMPs)	2 21.08.12	24 September 2012
Covering Letter		27 September 2012

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

11/LO/0999:	Please quote this number on all correspondence
-------------	--

Yours sincerely



pp

Dr Shelley Dolan

Chair

E-mail: NRESCommittee.London-Chelsea@nhs.net

Enclosures: List of names and professions of members who took part in the review

Copy to: Miss Jane Lawrence

NRES Committee London - Chelsea

Attendance at Sub-Committee of the REC meeting on 26 October 2012

Name	Profession	Capacity
Mrs Patricia Pank	Retired University Lecturer	Lay Plus
Dr Michael Schachter	Clinical Pharmacologist	Expert

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pp

Dr Shelley Dolan

Chair

E-mail: NRESCommittee.London-Chelsea@nhs.net

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NRES Committee London - Chelsea

Attendance at Sub-Committee of the REC meeting on 26 October 2012

Name	Profession	Capacity
Mrs Patricia Pank	Retired University Lecturer	Lay Plus
Dr Michael Schachter	Clinical Pharmacologist	Expert

Evidenced based guidelines for the management of palliative care needs of patients with advanced Progressive Idiopathic Fibrotic Interstitial Lung Disease (PIF-ILD)

Evidence and recommendations

1. Shortness of Breath

Dyspnea or shortness of breath is a common symptom in patients with PIF-ILD. It is experienced by around 70-91% of patients with IPF.^{1,2} Dyspnea is the most important limiting factor influencing the Health Related Quality of Life of patients with IPF.³ Patients may describe their dyspnea as fatigue⁴ and it is important to distinguish between these two symptoms. Patients with chronic lung disease report higher levels of fatigue when they have dyspnea and a more negative mood state.^{5,6} Dyspnoea is often multi-factorial and assessment of patients with dyspnea should involve detailed history taking and comprising physical, psychological and social domains.⁷ Any reversible cause such as infection should be treated. A randomised controlled trial by Zisman et al⁸ showed that oral sildenafil may improve dyspnea in IPF patients but this was not supported by a second randomised controlled trial by Jackson et al.⁹ Similarly, there is some preliminary data supporting the use of co-trimoxazole¹⁰ and colchicine¹¹ and D-penicillamine¹² in reducing shortness of breath. However, the evidence is low grade and therefore not included in our recommendations. There is low grade evidence for the use of prednisolone for the relief of breathlessness.^{13,14}

- Take detailed history including physical, social, psychological and social impact of breathlessness
- Treat any reversible causes of breathlessness (eg infection)
- Address any underlying psychosocial issues

Opioids

Opioids act on the CO₂-sensitive medullary respiratory centre, but may also act on other sites to help reduce the sensation of breathlessness.¹⁵ A Cochrane review has shown that opioids used orally or parentally help relieve breathlessness¹⁶ in patients with terminal disease. In addition, an open observational case series of end stage IPF patients treated with subcutaneous diamorphine had significant decreases in dyspnea and observed anxiety without any adverse effects on vital signs or oxygen saturation.¹⁷ There is no evidence at present to support the use of nebulised opioids for breathlessness.^{16,18} A number of observational studies have found no evidence that the use of opioids in appropriate doses hastens death in palliative care patients.^{19,20,21}

- Opioid naïve, morphine sulphate 2.5-5mg p.o. PRN
- If effective use morphine regularly
- For patients who are on regular opioids for pain relief, use 5-10mg immediate release oral morphine sulphate solution or one twelfth of the PRN dose for pain whichever is greater
- In patients who are unable to swallow, morphine may be given subcutaneously as PRN doses, or, if needed regularly, via a subcutaneous infusion at half the oral dose or one-third of the oral dose if using diamorphine.

Non-pharmacological interventions

An integrated approach of breathlessness intervention has been of proven benefit in COPD.²² Pulmonary rehabilitation programs involve aerobic conditioning, strength and flexibility training, educational lectures, nutritional interventions, and psychosocial support. There is evidence in IPF that pulmonary rehabilitation improves shortness of breath and quality of life.²³⁻²⁹ A prospective study of 17 IPF patients receiving a home based pulmonary rehabilitation program for 12 weeks showed a significant decrease in dyspnea, an increase in six minute walk test distance (6MWD) and general health related quality of life.³⁰ A randomised controlled trial of 34 IPF patients conducted by Holland et al²³ supported these findings. In addition, pulmonary rehabilitation ILD patients showed improvement in dyspnea and quality of life in a prospective observational study which included IPF, NSIP and IIP patients³¹ and quality of life and 6MWD in a randomised controlled trial conducted by Nishiyama et al.³² The Nishiyama trial did recruit patients with other aetiologies of pulmonary fibrosis so should be interpreted with caution. A prospective open label trial of a 8 week pulmonary rehabilitation out patient program using a COPD comparator by Kozu et al²⁹ found an improvement in dyspnoea and exercise capacity but there was less improvement in the IPF group. The benefits were well maintained in the COPD group at 6 months but were no longer present in the IPF group. The beneficial effects of pulmonary rehabilitation may be more pronounced in patients with worse baseline functional status.²⁶ Pulmonary rehabilitation may also help with the symptom of fatigue^{23,33} which has been reported in up to 97% of IPF patients² and is a major problem effecting their quality of life.⁶ Patients with advanced disease can benefit if they are selected appropriately and if realistic goals are set.³⁴ Pulmonary rehabilitation should be used in the majority of patients with IPF, but not using pulmonary rehabilitation may be a reasonable choice in a minority of patients who are not able.³⁵ Severe pulmonary hypertension has been considered a contraindication to participate in pulmonary rehabilitation, but with attention to the nature and intensity of exercise, these patients may be enrolled in an exercise program.³⁶

- Referral for pulmonary rehabilitation if available

A Cochrane review looking at non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases³⁷ found there was a high strength of evidence for neuro-muscular electrical stimulation and chest wall vibration in relieving breathlessness and moderate strength for the use of walking aids and breathing training. There was a low strength of evidence that acupuncture/acupressure is helpful and no evidence for the use of music. The authors felt that there was not enough data to judge the evidence for relaxation, fan, counselling and support, counselling and support with breathing-relaxation training, case management and psychotherapy. Most studies in this review were conducted in COPD patients and there were no studies containing PIF-ILD patients. As there may be a close link between psychosocial issues and shortness of breath, psychosocial interventions³⁷ such as counseling, cognitive behavioural therapy and psychotherapy may be useful in PIF-ILD patients.

- Early referral to breathlessness clinic or team: Palliative Care Clinical Nurse Specialist, physiotherapist and occupational therapist.

- Consider alternative therapies such as relaxation, acupuncture or aromatherapy
- Consider psychosocial interventions

Subjective dyspnea has been shown to not be related to pulmonary function parameters in IPF patients.⁶ That is, patients' perception of breathlessness is not associated with objective breathlessness measures.⁶ It is possible that the effect of cool air blowing on the face mediated by the trigeminal nerve may reduce the sensation of breathlessness³⁸ and the use of a hand-held fan has been shown to be effective in a number of studies³⁹⁻⁴¹ including a randomised control by Galbraith et al.⁴² These studies included a wide range of end stage respiratory diseases but mainly concentrated on COPD patients and there is no separate data available for PIF-ILD patients. However, on balance, it is appropriate to give a trial of a hand-held fan.

- All breathless patients should be offered and taught how to use a fan

Benzodiazepines

A Cochrane review of the use of benzodiazepines in the palliation of breathlessness found no evidence for their use in cancer, COPD and IPF patients.⁴³ However, as breathlessness is often associated with anxiety, they may be helpful to palliate dyspnea where anxiety is a component of the breathlessness.^{44 45} A trial of benzodiazepines may be appropriate but should be used third line after opioids and non-pharmacological measures.

- Lorazepam 0.5-1-2mg s.l. PRN
- Diazepam 2-5mg TDS p.o.
- If neither lorazepam nor diazepam can be taken orally, Midazolam 2.5-5mg s.c. PRN may be given

Oxygen

There are no data that directly inform the use of long-term oxygen therapy in patients with PIF-ILD. However, a study reported significant improvement in dyspnea with oxygen therapy in ILD patients.⁴⁶ In addition, retrospective assessment has shown improvements in dyspnea in IPF patients⁴⁷ and in a group of patients containing IPF and NSIP. (Visca ref) Oxygen has been shown to be superior to placebo in symptomatic, hypoxic, advanced cancer patients.¹⁵ Breathlessness is poorly correlated with hypoxia-patients may be hypoxic without feeling breathless and relief of hypoxia may not provide relief of breathlessness.⁴⁵ Interestingly, in a study by DeVries et al, there was no difference in quality of life of IPF patients using oxygen and those who did not.⁶ In addition, there are significant disadvantages to the use of oxygen: psychological dependence, inconvenience, interference with communication and restricting activities of daily living. However, short-burst oxygen should be considered for episodic breathlessness not relieved by other treatments in patients in palliative care.⁴⁸

- Oxygen should be used only after a former trial of its effectiveness. Short burst oxygen should be offered if adequate relief is not obtained by using the fan in combination with other pharmacological and non-pharmacological treatments.

Steroids

A study by Turner-Warwick¹⁴ showed subjective improvement in dyspnoea in 43% CFA patients treated with steroids. However, this was a retrospective review of case notes and it is possible may have included a mixed group of patients. In addition a randomised prospective study of UIP patients by Douglas et al describes a subjective improvement in both breathlessness and cough but no details of outcome measures are given.⁴⁹

Considering the high side-effect profile and the lack of evidence, they have not been recommended here. Other drugs which have been investigated include bosentan which had shown some improvement in a secondary endpoint of dyspnea and health related quality of life in a randomised control trial of IPF patients.⁵⁰ However, this was not supported in a later randomized controlled trial of over 600 biopsy confirmed IPF patients⁵¹ and has therefore not been included in our recommendations.

Nebulised normal saline

In studies where nebulised normal saline has been the placebo arm for nebulised morphine, the placebo group experienced a significant reduction in breathlessness^{52 53} A trial of nebulised saline may be appropriate.

- Normal saline 5mls nebulised 2-4 hourly or PRN

2. Cough

Cough is a common problem in IPF patients with 60-88% reporting it as a symptom.^{1 2 54} Women with cough are often troubled by stress incontinence and this may be one of their major concerns.⁵⁵ A French study in a mixed group of 28 ILD patients which included IPF patients, showed that stress incontinence was present in 50% of female patients with chronic cough compared to 7% of healthy controls.⁵⁶ All were ashamed of the symptom and 79% felt unable to mention it to their physician.⁵⁶

- Treat reversible causes eg infection, stop ACE inhibitor if appropriate, smoking cessation
- Assess full impact of cough

Rhinosinusitis is commonly associated with chronic cough and in the presence of prominent upper airway diseases a trial of a topical corticosteroid is recommended.⁵⁵

- First generation sedating antihistamine +/- oral decongestant

Mucolytics

Mucolytics should be considered if there is a chronic cough productive of sputum, and should be continued if there is symptomatic improvement.⁵⁷

- Nebulised saline-5mls PRN
- Physiotherapy if appropriate
- Carbocisteine 750mg TDS PO, then 1.5mg daily in divided doses
- N-acetyl cysteine 2-5mls (400-1000mg) made up to 5mls with normal saline for nebulized delivery via air

Reflux agents

Cough on eating, postprandially or on phonation may indicate reflux cough.⁵⁵ Proton Pump Inhibitors (PPI) are the treatment of choice for gastro-oesophageal reflux disease (GORD) related chronic cough and improves GORD related cough in 36-100% of patients.⁵⁸⁻⁶⁰ In addition, H2 antagonists have also been shown to improve GORD cough.⁶¹ However, full acid suppression may only be possible by bd PPI and nocturnal H2 antagonist.⁶² A prokinetic agent such as metoclopramide should be added if a diagnosis of oesophageal dysfunction is suspected.⁶³

- Proton pump inhibitors (PPIs) such as omeprazole 20–40 mg twice daily or equivalent taken before meals for at least 8 weeks even if the patient does not have reflux symptoms.
- Consider addition of a nocturnal H2 antagonist. Prokinetic agents such as metoclopramide 10 mg three times daily may be required in a proportion of patients.

Some patients with cough may benefit from surgical intervention such as fundoplication if appropriate.⁶⁴⁻⁶⁸

- Consider referral for fundoplication if appropriate

Steroids

One small study has shown that treatment with oral corticosteroids decreases cough severity and sensitivity in IPF patients.⁶⁹ In addition, a randomised prospective study looking at colchicine versus prednisolone noted a subjective improvement in cough but no details were given.⁴⁹

- Trial of high dose steroids- 40 mg/day prednisolone (stop if not beneficial as significant side effect profile)

Where reversible causes are treated/excluded, it would be appropriate to treat the cough as idiopathic using the following:

Cough suppressants

There is no evidence for the use of conventional anti-tussives in PIF-ILD. However, a trial may be appropriate.

- Simple linctus-5mls QDS
- Codeine linctus-30-60mg QDS

- Pholcodeine linctus-5mg/5ml:5-10mls 3-4 times daily for dry cough

Opioid receptors of the lung, pharynx and upper airways produce mucus in response to irritation. These receptors are blocked by oral opioids, as in the cough reflex centre in the brain⁷⁰ therefore opioids are useful as cough suppressants.^{70 71 72}

- Morphine Sulphate immediate release solution 2.5mg 4 hourly if morphine naïve, increase dose by 1/3 if already on morphine
- Methadone linctus 5-10mls nocte p.o. (recommend referral to palliative care team)

In addition, moguisteine and levodropropizine have been shown to have some efficacy in the cough associated with chronic respiratory disease reducing both daytime and night-time cough frequency.⁷³ This randomized controlled trial included pulmonary fibrosis patients (16% of cohort). However, data is not supplied separately for this group so should be interpreted with caution and these drugs are not readily available in the UK. Baclofen has also been shown to improve chronic refractory cough⁷⁴ possibly through increasing lower oesophageal tone and decreasing lower oesophageal opening or via the cough reflex. Other drugs used in preliminary trials and shown to be effective include carbamazepine⁷⁵, paroxetine⁷⁶, amitrytilline^{77 78}, gabapentin⁷⁹ and nebulised lignocaine (risk of aspiration).⁸⁰ However there is no evidence for their effectiveness in IPF patients. A preliminary study looking at the use of thalidomide in IPF has shown promising results⁸¹ and a phase III randomised placebo controlled trial is currently underway which may provide further information on its efficacy in IPF patients.⁸² In addition a preliminary study of interferon alpha lozenges has shown promising results.⁸³ However, further work is needed before recommendations can be made.

3. Pain (adapted from WHO analgesic ladder)

Pain and discomfort have been found to affect the quality of life of IPF patients.⁶ We would recommend following the WHO analgesic ladder. However, the use of NSAIDs should be considered carefully weighing up risk and benefit. They should be used with caution in patients with history of peptic ulcer disease, renal or hepatic impairment, heart failure or asthma, those on steroids, anticoagulants, SSRIs. There is some conflicting evidence about their use in the literature with some case studies linking the use of NSAIDs with ILD^{34 84 85}. However another case control study of 141 CFA patients showed no association⁵⁵

Step 1 Mild pain

Non-opioids

- Paracetamol- 500-1000mg every 4-6 hours
- NSAID- diclofenac 50mg TDS- Ensure a proton pump inhibitor is used alongside.

Step 2 Mild to moderate pain

Weak opioid + non-opioid from Step 1

- Codeine

- Dihydrocodeine
 - Tramadol-50-100mg QDS (max 400mg daily)
- +step 1 non-opioids

Step 3 Moderate to severe pain

- Morphine-starting dose 5-10mg po qds/PRN. Increase at 33%-50% increments. Subcutaneous dose is half of oral dose and if using diamorphine, use 1/3 of oral dose.

If pain is not controlled despite escalation of morphine or intolerable side effects then alternative opioids may be appropriate for which we would recommend advice from a Palliative Care Team.

Adjuvants such as neuropathic agents may be used at any step but we would recommend referral to the palliative care team.

4. Dyspepsia

An increased acid gastro-oesophageal reflux has been demonstrated in 36-94% of patients with IPF⁸⁶⁻⁹¹. The incidence in similar age groups in the general population has been shown to be less than 10%.⁹² Reflux symptoms have been shown to be present in 47-77% of IPF patients^{87-89 93 94} but there does not appear to be any correlation between IPF severity and reflux severity.⁸⁷ The typical symptoms of heartburn and regurgitation do not distinguish between those with and without reflux.^{86 89-91 93 94} Symptomatic and asymptomatic reflux may lead to worsening dyspnoea, cough and chest pain.^{88 90} Higher doses of PPIs and H2 antagonists than normal may be needed as it has been shown that treatment with standard doses of PPIs suppressed acid reflux in only 37% of patients with IPF.⁸⁷ Delayed gastric emptying, poor oesophageal peristalsis and dysfunctional oesophageal sphincters appear to be contributing factors.^{88-91 94} Prokinetics such as metoclopramide may reduce both acid and non-acid reflux.

- Proton pump inhibitors (PPIs) such as omeprazole 20–40 mg twice daily or equivalent taken before meals for at least 8 weeks even if the patient does not have reflux symptoms. Prokinetic agents such as metoclopramide 10 mg three times daily may be required in a proportion of patients.

A study of gastro-oesophageal reflux IPF patients showed that reflux in 50% was exclusively in the supine position.⁸⁸ A systematic review in the general population revealed that elevation of the head of the bed, sleeping in the left lateral decubitus position and weight loss were effective for patients with GORD.⁹⁵

- If appropriate, lifestyle adaptation

5. Constipation

There is no specific evidence on the treatment of constipation in PIF-ILD patients. The guidance that follows has been adapted from cancer studies.

All patients on opioids should be started on a laxative. There is no proven correlation between increasing doses of opioids and the need for escalating doses of laxatives. The necessity for increasing doses of laxatives will depend on the patients response.⁹⁶

- Encourage oral fluids
- Make diet modifications- increase fibre and improve hydration
- Milpar 10-20mls BD +Senna 2-4 tablets BD⁹⁷

Or

- Docusate 2-4 capsules BD⁹⁸ +Bisacodyl tablets 5-10mgs BD also available in suppository form

Rectal intervention⁹⁸

If faeces palpable on PR

- Glycerine suppositories (2) or microlette or phosphate enema
- If colonic impaction- high arachis oil enema (avoid in patients with nut allergy) followed by phosphate enema the following morning.

6. Nausea/vomiting

There is no specific evidence on the treatment of constipation in PIF-ILD patients. The guidance that follows has been adapted from cancer studies.

- Always consider non drug treatment eg control of malodour, avoidance of large meals, avoidance of food smells that may precipitate nausea
- If possible discontinue any drugs thought to be responsible for nausea and vomiting.
- Identify and treat any underlying causes of gastrointestinal problems (constipation, gastritis or reflux), pharyngeal irritation (candida, difficulty expectorating sputum), psychomatic fears (anxiety or fear), pain

Consider anti-emetic:

- Metaclopramide-10-20mg TDS p.o. or s.c.
Prokinetic agent⁹⁹ therefore good if patient constipated.

OR

- Cyclizine
50mg TDS p.o. or 150mg via CSCI over 24 hours
+/-

- Haloperidol¹⁰⁰
1.5mg-3mg b.d. or 1.5-5mg via CSCI over 24 hours

7. Depression

In 41 patients with IPF, De Vries and colleagues reported that approximately 25% experienced depressive symptoms.⁶ Another small study in IPF found that scores for depression and anxiety were higher than in healthy controls but were not high enough to suggest clinically significant depression or anxiety.¹⁰¹ There are no specific studies looking at the management of depression in IPF patients. The depression guidelines developed by Rayner et al for palliative care patients have been adapted.¹⁰²

When assessing depression, it is important to take a thorough psychiatric history. It should not be assumed that this is the first episode of depression, precipitated by being terminally ill. Patients with a history of depression are much more likely to have a further episode. Information about previous episodes of depression and previous treatments should be sought.¹⁰²

In palliative care, it is particularly difficult to distinguish depression from normal sadness or adjustment disorder relating to declining health and fear of death. Take into account the patient's personality, family circumstances and the history of their illness and coping. If there is uncertainty about the diagnosis, refer the patient to a mental health specialist.¹⁰²

Pulmonary rehabilitation is known to have positive psychosocial benefits that help patients understand their disease and mitigate anxiety and depression.^{103 104}

Both SSRIs and TCAs are effective in the treatment of depression in physical illness when compared to placebo.¹⁰⁵ Antidepressants improved depressive symptoms within 4-5 weeks of treatment, and this benefit persists after 18 weeks.¹⁰⁵ There is evidence that CBT in palliative care can improve some outcomes.¹⁰² The decision to prescribe antidepressants should take account of patients' preferences, prognosis, symptoms, and possible interactions with other medicines they are taking.¹⁰⁵

Mild depression or adjustment disorder¹⁰²

First-line treatment:

- Provide good palliative care
- Assess quality of relationships with significant others. Facilitate communication between family members
- Consider a guided self-help programme that consists of provision of appropriate written materials and support
- Consider a brief psychological intervention (CBT (shown to improve depression and health status in COPD¹⁵), problem-solving therapy, counselling)

If symptoms persist (or the patient has a history of moderate/ severe depression):

Where mild depression persists after other intervention, consider use of an antidepressant.

Moderate depression¹⁰²

First-line treatment:

- Do all recommended as first-line treatment for mild depression
- Antidepressant medication and/ or CBT

Given the lack of evidence on a clearly superior approach for moderate depression, treatment decisions should be based on patient and clinician preference. Choice of antidepressant may be different for patients with short prognosis. Consider the use of tricyclic antidepressants (TCAs) or mirtazapine, which may have earlier onset of action than SSRIs in patients with advanced disease and in whom improvement in mood and quality of life is the main focus of care. In patients who are not end stage, tricyclics and related antidepressants should be avoided as there has been shown to be an association between CFA and exposure to tricyclic and related antidepressants (not amitriptyline) particularly imipramine and dothiepin.⁵⁵

Antidepressants

- Mirtazapine- 15-45mg/day (max 45mg/day)
- Sertraline-(SSRI)- 50mg/day (max 200mg/day)
- Citalopram (SSRI)- 20-40mg/day (max 60mg/day)
- Amitriptyline (TCA)- 75-200mg/day (max 200mg/day)

If symptoms persist:

Assess compliance to treatment

Consider switching to a different antidepressant of the same or different class

Consider combining antidepressant treatment and CBT

Reassess psychosocial environment, e.g. family/marital relationships

8. Anxiety

Anxiety and panic attacks are more common place in patients with advanced respiratory disease.^{106 107 108 109} A review of the literature in palliative care patients has shown that

psychological, social and medical conditions may lead to panic in dying patients.¹¹⁰

Anxiety may contribute to depressive symptoms or be a product of poor coping mechanisms.¹⁰⁹ Other factors such as social isolation and sub optimal palliation may also contribute.¹⁰⁹

- Take a full history to assess main factors contributing to anxiety.
- Address any psychosocial concerns
- Provide good palliative care

Both TCAs¹¹¹ and SSRIs^{112 113} are effective in the treatment of panic disorders though there is no direct evidence in PIF-ILD patients.

Anxiolytics

- Sertraline-(SSRI)- 50mg/day (max 200mg/day)

- Citalopram (SSRI)- 20-40mg/day (max 60mg/day)
- Amitriptyline (TCA)- 75-200mg/day (max 200mg/day)

Non-pharmacological methods such as relaxation therapy and breathing exercises are effective in palliation of anxiety and should be used in conjunction with pharmacological methods to improve effectiveness.¹¹⁴

- Referral for relaxation therapy and breathing exercises

There is no evidence for the use of benzodiazepines in the anxiety management of PIF-ILD patients. However, a short trial may be appropriate.

Benzodiazepines:

- Lorazepam 0.5-1-2mg s.l. PRN
- Diazepam 2-5mg p.o.TDS
- Midazolam 2.5-5mg s.c. PRN (if the oral route is not available)

9. Insomnia/sleep disturbance

Snoring is a common place problem in IPF patients with one study showing 86% habitually doing so.¹¹⁵ Patients frequently have sleep apnoea (57-88%¹¹⁵⁻¹¹⁷) which may contribute to daytime fatigue found in 61-100% of IPF patients.^{115 116 118} Sleep apnoea may be associated with obesity but is found in IPF patients who are not overweight.^{115 119}

- Consider weight loss measures if appropriate

In addition, insomnia/sleep difficulty is commonplace in IPF patients¹¹⁹ (58-78%^{2 120}). The frequency and the importance of hypoventilation during sleep are unclear.¹²¹ A study of IPF patients has shown that 78% of a sample of 49 patients reported insomnia with 41% reporting moderate to severe levels.¹²⁰ Poor sleep quality and daytime sleepiness are associated with impairment of physical and social functioning¹¹⁸ and poor quality of life^{118 119} but not with pulmonary function test parameters.¹¹⁹

It is possible that insomnia/sleep disturbance is contributed to by depression/anxiety. However poor sleep quality in IPF patients has also been shown to adversely impact on their emotional well-being.¹¹⁹ In addition other symptoms such as cough may disturb sleep.

- Optimise palliation of anxiety/depression and other symptoms

There are no studies looking at the use of night sedation in PIF-ILD patients. A short trial may be appropriate.

- Consider night time sedation e.g. zopiclone 3.75-7.5mg o.n. if appropriate.

All patients:**Optimising palliative care and support**¹⁰²

- Take account of psychosocial needs as well as physical ones.
- Consider referral to palliative care for symptom control, physical, emotional, social and spiritual support.
- Address potential deficits in social support which might happen in patients whose disabilities could impair opportunities to socialise (e.g. dysphasic, deaf, poor mobility).
- Assess patients' coping strategies. Where necessary, facilitate the development of new effective strategies to help patients regain a sense of control (e.g. staying active, taking a walk, engaging in social relationships, finding meaning in events).
- Advise patients and their families where to seek financial and practical support (e.g. advice on housing and employment issues, state benefits, mobility (e.g. disabled parking), help with personal care, cleaning and shopping).
- Self-help and support groups can be a source of valuable advice and peer support. Inform patients of the services available to them and advise them to attend.
- Health professionals should be aware that some patients may have spiritual needs, and arrange support from appropriate spiritual advisers (e.g. chaplains) when necessary.
- Introduction of suitable palliative care frameworks such as the Gold Standards Framework¹²² and Liverpool Care Pathway¹²³ at the end of life should be considered where appropriate.
- Advance care planning including documentation of Preferred Place of Care and Preferred Place of Death should occur in all patients.

Discussion

These are the first guidelines for managing the palliative care needs of patients with PIF-ILD. In some areas, the evidence is sparse and the guidelines have therefore been adapted from other end-stage respiratory diseases or the cancer group. However in other areas (e.g. pulmonary rehabilitation) there is a growing body of evidence that interventions do improve symptom control in these patients. Appropriate and validated outcome measures should be used to ensure that the palliative care needs of these patients are accurately assessed and recorded. These guidelines should then be used alongside respiratory interventions to ensure that the holistic needs of these patients are met.

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APPENDIX C RCT protocol



A fast-track randomised controlled trial to evaluate a Hospita2Home palliative care service for patients with advanced Progressive Idiopathic Fibrotic Interstitial Lung Disease

Protocol Version 1.4 08/06/11

Short Title: *H2H PIF-ILD study*

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Version 1.4 08/06/11

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1. Background

Background

There are at least 2,000 new cases of Progressive Idiopathic Fibrotic Interstitial Lung Disease (PIF-ILD) each year in England and Wales, with a similar number of deaths each year (1;2). The most common disease in this group is idiopathic pulmonary fibrosis (IPF). Data from UK general practice records(3) suggest that the 12-month period prevalence of PIF-ILD is 15–18/100 000 person-years and, based on a median survival from diagnosis in the UK of approximately 3 years (4;5) this equates with an estimated incidence of 5/100 000 person years. There is evidence from death certificate data that the incidence is increasing (1;2). Only a minority of patients are suitable for lung transplantation and there are no other significant treatment options once the disease is advanced and irreversible.(6) Physicians managing these patients need to focus on symptom control and maximisation of quality of life.(7)

Currently, these patients achieve poor symptom control (8-11), are reported to have poor quality of life (12) and are being admitted acutely to the inpatient setting (Appendix 1a).

Studies have shown the majority (49-78%) of patients would rather die at home. (13) However, death statistics show that the number of home deaths are falling, and this is more pronounced in non-cancer related deaths. (14)

Following a systematic review of factors influencing death at home (15) Gomes and Higginson advocated that any action to enable people to die at home should prioritise ways of empowering families and public education, balanced with a continuing effort to improve home-based models of care, early risk assessment and generalist training in palliative care.

Case conferencing can provide a mechanism to enhance co-ordination between terminally ill patients, their carers and health care professionals. (16) A randomised controlled trial (16) in the community palliative care setting in Australia showed that patients and health care professionals find the case conference a positive experience, and that it can achieve improved pain control and resource utilisation. (16;17) In the UK, a pilot study of the Hospital2Home (H2H) model in cancer patients has shown that 80% of 121 patients were enabled to die at home when a case conference was used.(18) However, high quality research into use of the case conference model in the UK to interface between acute and community providers in end-of-life care is lacking, including how this intervention may affect symptom control, anticipatory care and quality of life. This research aims to address each of these issues.

There is limited evidence to guide palliation of patients with PIF-ILD (8-11) and other non-malignant lung diseases. Studying this group and developing a model of care at the end of life, will help inform us about other disease groups with similar disease journeys (e.g. cystic fibrosis). This study will act as a template for the development of appropriate interventions for other non-malignant diseases and will help inform their end-of-life management.

The trial will be conducted in compliance with the protocol, standard operating procedures, policies, local R&D management guidance, Good Clinical Practice including the Research Governance Framework 2005 (2nd edition) and other applicable regulatory requirement(s).

2. Rationale

In the UK, a pilot study of the Hospital2Home model in cancer patients has shown that 80% of 121 patients were enabled to die at home when a case conference was used.⁽¹⁸⁾ However, high quality research into use of the case conference model in the UK to interface between acute and community providers in end-of-life care is lacking, including how this intervention may affect symptom control, anticipatory care and quality of life. In addition, there is no research in this area in the non-malignant setting. This research aims to address each of these issues.

This study is the basis of a PhD for one of the investigators

3. Hypothesis/research question

What is the impact of the H2H intervention on symptom control in PIF-ILD patients in the last year of life compared to standard best practice?

We hypothesise that H2H will result in improved symptom control and quality of life and may be more cost-effective than standard best practice.

4. Aims

Primary-

- To assess whether the complex intervention of evidence based guidelines and case conference (collectively termed Hospital2Home-H2H) improves symptoms of patients with PIF-ILD in the last year of life.

Secondary

- To compare patient and carer reported POS scores
- To assess whether H2H improves quality of life, informal caregiver burden and use and costs of formal health and social care services and prognosis.
- To determine whether H2H allows people to achieve their preferred place of care and death.
- To evaluate clinical use of a dichotomous staging system to identify patients with PIF-ILD for whom proactive planning of end-of-life care is now appropriate.
- To evaluate evidence based guidelines for the palliative management of patients with severe PIF-ILD.

5. Study Design (Phase II of the Medical Research Council framework⁽¹⁹⁾ for the development of complex interventions)

A fast track pragmatic randomised controlled trial evaluating a H2H intervention for patients with severe PIF-ILD. (appendix 1b).

Patients will be identified by the respiratory and palliative care teams. After providing consent and baseline interview, patients at RBH site meeting inclusion criteria will be allocated to fast track or waiting list by independent off-site randomisation. Randomisation will be provided by The Institute of Cancer Research - Clinical Trials and Statistics Unit (ICR-CTSU). The ICR-CTSU will provide a unique randomisation number

(Trial ID) for each patient together with the allocated treatment code. Treatment allocation (fast track/waiting list group) will be by computer generated random permuted blocks. If patients are randomised to fast-track, their information will be passed to the H2H nurse to organise a case conference within one week of discharge. If patients are in the control arm, they will continue to receive Standard Best Practice (SBP) and their data will be held by the researcher until after the second interview (4 weeks). After this time, they will be contacted by the H2H nurse to receive the intervention and will be interviewed and followed up as for the fast track group.

Standard best practice (SBP)

Patients affected by PIF-ILD within the study area receive a range of services. These are available to all those who receive the H2H intervention immediately or after a delay. Services include general practitioners, physiotherapy and respiratory services (including specialist rehabilitation services) and community palliative care teams. All will have seen a respiratory physician at RBH preceding referral and will remain under their care with access to in-patient care as appropriate.

The Hospital2Home Service (H2H)- the intervention

H2H will be offered in addition to the SBP services outlined above. H2H aims to complement the existing local services and not to duplicate or replace them. This intervention is a new multiprofessional, patient centered meeting or case conference that is organised for people nearing the end-of-life. In recent months we have been conducting a review of the literature and interviews of patients, informal caregivers and health professionals. This has enabled us to start developing evidenced based guidelines for the management of the physical, psychological, spiritual and end of life-planning needs for these patients. These guidelines (still under development) will be used in the H2H case conference. The written guidelines will act as a supplement to the actual assessment. With the patients consent, a case conference will be organised in their home (or place of their choice). The patient, informal caregiver, H2H CNS, GP, district nurse, social worker and community palliative care nurse are invited to attend. Current and anticipated care needs are discussed, and an action plan is agreed allocating a responsible health care professional for each item. During the case conference, individualised care plans will be made. The care plan provides a quality comprehensive Palliative Care assessment (appendix 2). This is then communicated with local services, both primary and specialist teams resulting in streamlining of transfer of data and codifying responsibility for the patient, hospital and community care professionals. The aim is to enable improved symptom control, quality of life, crisis prevention and decreased hospital admissions. In addition, this intervention will aim to manage uncertainty by facilitating early discussion about disease progression, improving communication and addressing end of life planning needs.

The Royal Brompton Marie Curie H2H CNS will deliver teaching on the use of the evidence-based guidelines and will follow up each case conference (at 2 weeks, 1 month and 2 months) to assure quality and control of the care received.

The guidelines will permit a structured and evidence based practice in delivering palliative care where there has previously been none. The ongoing palliative care of these patients will be delivered by the community palliative care team as deemed appropriate by them.

6. Outcome Measures and End Points

The primary endpoint for this study will be change in POS outcomes at 4 weeks compared to baseline. For an individual patient, participation in the study ends either when they withdraw, become too unwell to participate in serial interviews, complete all contacts in follow up, or they die. For the informal caregiver, participation in the study ends either when they themselves decide to withdraw, they complete all follow up or they die. If any participant becomes too unwell and unable to complete assessment, loses capacity or dies, they will be removed from the study. However, data already collected will be retained and used in analysis. If the intervention has been delivered and the patient has become too unwell to continue in the study, the informal caregiver's consent will be reconfirmed and data will continue to be collected from the informal caregiver alone until the patient dies.

All patients (in both groups) will have information collected at baseline, 4 weeks and 8 weeks after randomisation. The H2H case conference will occur within a week of the baseline interview for the intervention group and within a week of the 4 week information collection for the waiting list group. Each patient will then be followed to the point of death to document place of death.

Primary outcome

The primary outcome will be to compare the change in POS scores recorded at week 4 and baseline for each group; POS scores evaluate symptoms and palliative concerns using the Palliative Care Outcome Scale (POS)(20) (appendix 11). This comprises eight questions on anxiety, patient and informal caregiver concerns, and practical needs, each rated 0-4. This scoring system will ensure that there is some ongoing data available if the patient becomes unwell and is no longer able to complete the study.

Secondary outcomes

Secondary outcomes will include comparison of the patient and informal caregiver POS in this study to see how inter-changeable/reliable the 2 assessments are.

The other secondary outcomes will focus on quality of life. (appendix 3) At each interview, service use questions will be asked which will record the frequency and types of health/social services received (see appendix 4, 12 &13) in order that an accurate evaluation of cost of care per patient can be made. In addition semi-structured qualitative interviews will be conducted with patients, informal caregivers and health professionals. Prompts will include views of the case conference, the guidelines and what level of input was needed after the case conference. A record will be made of when and where the patient dies.

Other data collected

Face-to-face interviews with patients and informal caregivers, supplemented by hospital notes will be used to obtain demographic information such as age, sex, ethnicity, co-morbidity and duration of illness. This will allow the study population to be accurately described, enabling later assessment of applicability of the data to other populations and settings.

Sample size

This is a phase 2 study that will demonstrate feasibility and acceptability of the proposed new programme of care and will inform the design and analysis of a phase 3 trial. At present there is no robust data to enable calculation of precise sample size needed to show a significant change in POS scores between each arm. As such interpretation of

the analysis must be treated with caution but will be helpful in hypothesis generating and in providing estimates of effect size for the phase 3 trial.

We anticipate recruiting 26 patients per group ie 52 in all. Based on the local patient numbers, we estimate to identify 2 patients per week, and recruit and retain at least 1 each week giving 52 patients in one year. We anticipate that this number is sufficient to estimate the change in POS score between baseline and 4 weeks with reasonable precision. (Assuming a standard deviation of 2, a 95% confidence interval for the difference between the intervention and usual care group would be 2.2 units wide ie mean difference \pm 1.1 units, which we judge to be sufficiently precise). The POS data are likely to be skew and the study will allow time to identify the most appropriate way to analyse these data for a later phase 3 study.

As part of this study we will check the validity and reliability of the modifications to POS.

We aim to recruit an initial 15 patients (5 patients, 5 informal caregivers and 5 health professionals) who have been involved in the study for qualitative interviews. The data will be analysed and further participants recruited if needed.

Data audit

To examine the feasibility of the trial methodology, the following will be examined: recruitment rates into the trial, response rates to the individual questionnaires and comments relating to the trial functioning. Cost data will be collected at baseline (before randomisation) and at 4, and 8 weeks.

6. Inclusion/ Exclusion Criteria

Inclusion criteria

Patients

- i) Clinical diagnosis of PIF-ILD and a 30% survival at 1 year according to the validated prognostic tool developed by Professor Wells.(Appendix 5)
- ii) Aged 18 years or over
- iii) Any patient who does not meet any of the exclusion criteria

Carers

- i) The informal caregivers of patients specified above, who can be significant others, relatives, friends or neighbours
- ii) Aged 18 years or over
- iii) Any carer who does not meet the exclusion criteria

Health professional

Primary health professional in contact with patient able to give consent

Exclusion criteria

Patients/informal caregiver

- i) Any patient/ informal caregiver unable to give informed consent
- ii) Any patient/informal caregiver less than 18 years of age
- iii) Participants who are unable to understand/speak English
- iv) Participants who are remaining as an inpatient in the hospital or being transferred to another inpatient facility (eg hospice unit, for terminal care)

v) Participants whose prognosis is less than 1 week or judged too unwell by the research team to take part in serial interviews

- **Subject Withdrawal Criteria**
If any participant becomes unwell and unable to complete assessment, loses capacity or dies, they will be removed from the study.

7. Data Acquisition and Storage

The patient, informal carer and community health care professional questionnaire clinical record files will all be completed by a researcher at the time of assessment rather than relying on participants to complete questionnaires and return them. This method has been chosen to minimise missing data. The data will then be entered into a secure clinical research system (CRS) database in the RMH System.

8. Data Analysis

The change in POS score (Baseline to 4 Week) will be compared between groups. Unpaired t-test will be used to compare POS symptom scores between the fast-track and waiting list group at both 4 weeks (before the waiting list group receives the intervention) and 8 weeks. If assumptions of normality are not met the data will be log transformed or use non-parametric method of analysis. Summary of POS scores of all patients' in each group will be reported at each time point.

We will also perform secondary analyses using analysis of covariance (ANCOVA) to examine group differences in 4 and 8 week POS values adjusted for baseline values. We shall examine trends in POS values across time as a longitudinal analysis using a linear mixed model. The profile of the POS scores over the time points will be modeled together with a modeling of the occurrence of (possibly informative) missing values. The analysis will adjust for baseline POS and include age, gender and degree of disease as candidate predictive variables.

Using Bland-Altman graphical and overall agreement calculation method, patients' and caregiver' POS scores will be compared. The overall agreement and its' 95% confidence interval will be reported.

Data on resource use will be combined with unit cost data (21) to provide estimate of overall costs per participant in each group. Following Gomes et al (22) suggestion, cost will be assessed using a broad perspective- including costs to health, social, and voluntary services and informal caregivers. Data regarding the use of health and social services will be collected at each interview. These will take into account salaries, overheads, training and the ratio of direct patient contact time to non-contact time.

The qualitative interviews will be audio-recorded, transcribed verbatim, and entered into NVivo 9.0. The interview data will be initially analysed for themes by hand using the constant comparative approach, and then cross-checked and refined using NVivo. Data will be initially coded as 'free nodes', and these will then be grouped into broader themes. Dual coding will be conducted and cross checked for accuracy. The framework approach will be used to analyse the qualitative data.

9. Study Organisation/ Trial Monitoring and Management Strategy

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The study will be conducted in accordance with Good Clinical Practice, and the relevant national legislation. The study is being submitted to the Local Committee for Clinical Research.

The chief investigator will be responsible for overseeing the conduct of the study, and for dissemination of the results of the study. A report will be written and sent to all participants request to have feedback

Research staff from the Royal Marsden and Royal Brompton Hospital palliative care department will be responsible for screening patients and obtaining consent. The H2H nurse will be based at the Royal Brompton Hospital (funding received from Marie Curie) and will deliver the intervention full time. The research fellow (Dr Sabrina Bajwah) will conduct the interviews and collect the data via phone- full time. The CI Julia Riley will contribute 4 hours per week to the project. Co-investigators will contribute as needed.

The research fellow or trial coordinator will audit a sample of the data collection forms to ensure they are complete and accurate. The statistician will facilitate 3 monthly review of the electronic data by the chief investigator to confirm the accuracy of data collection and storage. The research fellow will be responsible for ensuring a timely response to any problems that arise with practicalities of the study conduct.

A Project Advisory Group consisting of the co-applicants and collaborators will meet quarterly and ad-hoc to review progress. Additional members of the PAG will include:

- A community Palliative Care clinical nurse specialist from St Joseph's Hospice, Hackney. (Katie Mitchell)
- ILD clinical nurse specialist (Lucy Pigram).
- Patient (current attender at RBH).

Clinical team versus Research team

Both teams are entirely separate for the purpose of this study. The clinical Hospital2Home specialist sister at the Royal Brompton site will be responsible for the daily running of the case conferences. The respiratory and palliative care clinical teams will not be involved in the study, other than identifying patients to be approached by the research team. The co-investigators (and anyone they supervise) will be responsible for the assessment process, and the research fellow for the overall study management and coordination. The research team will not be involved in the clinical treatment of the patient population.

It is recognised that, in end of life care, research staff can experience similar 'burn out' to clinical staff, and the stress of interviewing terminally ill patients, observing their decline and eventual death builds up over time. Therefore, monthly team meetings will be scheduled so staff can reflect and share concerns, and the research staff with direct participant contact will attend training on self-care, and will have access to additional professional support if needed.

- Start date
01/08/11
- Study Completion
01/11/12
- Follow up plan

Patients will be followed up until death to note the place of death (non-interventional)

10. Adverse Events

All the questionnaires being used a validated tools, and have been previously been tested on populations similar to the study population. However, it is recognised that the completion of such questionnaire tools may for some participants or carers cause distress or unmask psychological states of concern

Adverse Event Monitoring and Reporting

After any interview adequate time will be allowed to check the impact and effect of the interview on the interviewee. They will also be directed to the appropriate source of health/social care professional as necessary.

If necessary, the researcher will provide the interviewee with relevant information about local counselling services, and with the interviewee's consent inform their GP/community medical teams of any concerns.

If the researcher has a high level of concern about the participant after the interview this will be urgently discussed with the principal investigator, and the clinical team to decide the most appropriate course of action.

All concerns of this nature will be documented in the clinical record file for the patient or carer, and the frequency of these concerns audited.

If the research team feel it is in the participants or informal carers interest to be withdrawn from the study this will be delicately communicated to them, and they will be withdrawn.

11. Other Statistical Considerations

- Number of patients- We expect to recruit 26 patients per group for the RCT. Based on the local patient numbers, we estimate to identify 2 patients per week, and recruit at least 1 each week. Recruitment over 1 year will provide 52 patients which should give us a sufficient indication whether differences between groups emerge. As this is a pilot study there is no formal sample size calculation but this is thought to be sufficient to assess feasibility of the study and inform a subsequent phase 3 study. Initially, 15 participants will be recruited for the qualitative work (5 patients, 5 informal caregivers, 5 health professionals).
- Data Monitoring Committee
Quantitative data will be entered into the RMH clinical research system by the research team and will be managed by the researcher and statistician at Royal Marsden Hospital with regular auditing of data integrity as above. The independent data monitoring committee will meet 6 monthly and will be provided with a summary report from the statistician and summary of SAE data from the trial coordinator/researcher. The committee will comprise a clinician (Dr John Williams) a statistician (Kjell Pennert) and information governance representative (Prof Michael Thick).
- Missing data for questionnaires will be minimised by the research team completing the questionnaires with the patient/informal caregiver, and reviewing all questionnaires for missing data before the end of that contact to double check data has not been accidentally missed.

12. Regulatory & Ethics Committee Approval

Every precaution will be taken throughout the study to ensure a duty of care to research participants and to respect their rights and autonomy. The trial will be carried out in accordance with the Declaration of Helsinki (1996).

The research has been planned to:

- Minimise the distress to participants by ensuring the researcher and H2H nurse are clear about their roles and boundaries of the study.
- Ensure help is available for participants when required.
- It is recognised that, in end of life care, research staff can experience similar "burn out" to clinical staff, and the stress of interviewing terminally ill patients, observing their decline and eventual death builds up over time.(24) Therefore, monthly team meetings will be scheduled so staff can reflect and share concerns, and the research staff with direct participant contact will attend training on self-care, and will have access to additional professional support if needed.
- We will seek and obtain informed consent from those who wish to participate in the study in line with the Trust's Consent to Examination or Treatment Policy (325) All participants will be able to decline to be interviewed/observed without prejudice to their care/treatment.
- All attempts will be made to anonymise data. All research staff will abide by the Data Protection Act 1998 and also in accordance with the CONFIDENTIALITY CODE OF PRACTICE AND DATA PROTECTION POLICY AND PROCEDURE (277)
- Data will be stored securely in line with GCP.

13. Data Handling and Record Keeping

All data relating to the study will be treated as confidential. All data from the study will be handled in accordance to trust policy and the Data Protection Act 1998.

The record forms will be anonymised and kept in locked secure cupboards. Computer generated files will be backed up according to The Royal Marsden Hospital back up policy. The record and computer files will be kept for a minimum of 5 years.

The investigators will permit study-related monitoring, audits and regulatory inspections providing direct access to source data and documents for this purpose

14. Financing, Indemnity & Insurance

The study will be financed by the Royal Marsden and Royal Brompton Palliative Care Research Fund

- An application has been made to the Marie Curie end of life call. This will cover the running cost of the study, including statistical support, data management and health economics support. A previous application was unsuccessful but received largely positive comments in peer review (appendix 9 & 10)

The Royal Marsden NHS Foundation Trust is the sponsor of this study

13. Publication Policy

Data from this study will be submitted for publication in peer review journals and presented at relevant conferences. All presentations and publications arising from this research study require authorisation from the Chief Investigator, Dr Julia Riley. The chief investigator will review all publications prior to submission.

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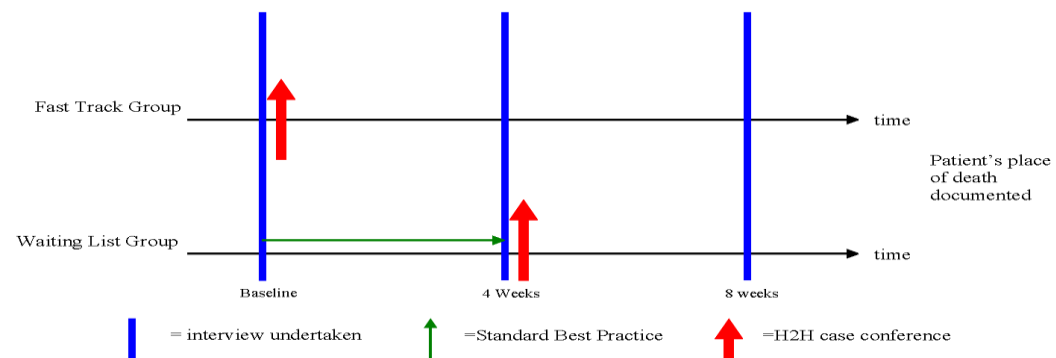
Appendix C1a Table showing admissions to RBH

Patients with fibrotic lung disease admitted to the Royal Brompton Hospital in 2009

	NO. OF PATIENTS	NO. OF ADMISSIONS	MEAN LENGTH OF STAY (DAYS)	TOTAL NUMBER OF INPATIENT DAYS	NO. OF DEATHS
In patient	154	325- 63 had multiple admissions (avg 2-4)	5.15	1,674	33

Appendix C1b Figure of study design

Fast track RCT design and timing of intervention and outcome measurements



Appendix C2a Care plan for H2H case conference

[Type text]

[Type text]

Participant id:

Care Plan for Royal Brompton Hospital2Home Patient

Issue/problem	Problem Codes	Patient goals of care and Management goals	Actions required	Person/People responsible	Review date

- Problem Codes**
1. Breathlessness
 2. Other symptom control (e.g. cough, fatigue, pain)
 3. Functional issue (e.g. difficulty mobilising, assistance with showering, assistance with taking medications)
 4. Psychological distress (e.g. depression, anger, guilt)
 5. Social issue (e.g. carer coping, carer availability, increasing dependence, change in relationships)
 6. Spiritual concern (e.g. religious issues, existential issues)
 7. Advance care planning/information need

Name of nurse completing.....

Designation.....

Signature.....

Date and time.....

[Type text]

Participant id:.....

[Type text]

Care Plan for Royal Brompton Hospital2Home Patient

Issue/problem	Problem Codes	Patient goals of care and Management goals	Actions required	Person/People responsible	Review date

Problem Codes

1. Breathlessness
2. Other symptom control (e.g. cough, fatigue, pain)
3. Functional issue (e.g. difficulty mobilising, assistance with showering, assistance with taking medications)
4. Psychological distress (e.g. depression, anger, guilt)
5. Social issue (e.g. carer coping, carer availability, increasing dependence, change in relationships)
6. Spiritual concern (e.g. religious issues, existential issues)
7. Advance care planning/information need

Name of nurse completing.....

Designation.....

Signature.....

Participant id.....

Case conference form for Hospital2Home patient
--

Date of Case Conference ____ / ____ / ____

Start time	<input type="text"/>	<input type="text"/>	:	<input type="text"/>	<input type="text"/>	End time	<input type="text"/>	<input type="text"/>	:	<input type="text"/>	<input type="text"/>
------------	----------------------	----------------------	---	----------------------	----------------------	----------	----------------------	----------------------	---	----------------------	----------------------

Patient consent obtained and documented	Yes	<input type="text"/>	No	<input type="text"/>	N/A	<input type="text"/>
Carer consent obtained and documented	Yes	<input type="text"/>	No	<input type="text"/>	N/A	<input type="text"/>
GP has agreed to attend case conference	Yes	<input type="text"/>	No	<input type="text"/>		
Copy of RBH community nursing referral form	Yes	<input type="text"/>	No	<input type="text"/>	N/A	<input type="text"/>
Copy of RBH medical discharge summary	Yes	<input type="text"/>	No	<input type="text"/>	N/A	<input type="text"/>
Copy of specialist palliative care referral	Yes	<input type="text"/>	No	<input type="text"/>	N/A	<input type="text"/>
Copy of Continuing Care form	Yes	<input type="text"/>	No	<input type="text"/>	N/A	<input type="text"/>

Persons attending the case conference

Name	Discipline	Organisation	Phone	Fax	Copy sent

Participant id.....

Current medication(s) including name, dose and frequency:

Drug	Dose	Route	Frequency	Drug	Dose	Route	Frequency
RBH Pharmacist Signature			Name			Date and Time	
Has the pharmacist completed and given the patient 'A guide to your medicines sheet'? (Delete as appropriate)						Yes / No	

Palliative Care Plan

Optional, include if appropriate

Has the patient expressed any wishes/instructions concerning matters related to their future care or death (with completion of the preferred priorities of care document).

Yes ☐ No ☐

Comments:

If yes, have the appropriate organisations been notified for e.g. hospice, emergency services.

Yes ☐ No ☐

Comments:

Participant id.....

Palliative Performance Scale at time of case conference

Palliative Performance Scale					
%	Ambulation	Activity and evidence of disease	Self-care	Intake	Level of consciousness
100	Full	Normal activity No evidence of disease	Full	Normal	Full
90	Full	Normal activity Some evidence of disease	Full	Normal	Full
80	Full	Normal activity with effort Some evidence of disease	Full	Normal or reduced	Full
70	Reduced	Unable to do normal job/work Some evidence of disease	Full	Normal or reduced	Full
60	Reduced	Unable to do hobby/house work Significant disease	Occasional assistance necessary	Normal or reduced	Full or confusion
50	Mainly sit/lie	Unable to do any work Extensive disease	Considerable assistance required	Normal or reduced	Full or confusion
40	Mainly in bed	As above	Mainly assistance	Normal or reduced	Full or drowsy or confusion
30	Totally bed bound	As above	Total care	Reduced	Full or drowsy or confusion
20	As above	As above	Total care	Minimal sips	Full or drowsy or confusion
10	As above	As above	Total care	Mouth care only	Drowsy or coma
0	Death	-	-	-	-

Plan for Documentation

Care plan prepared Yes ☐ No ☐

H2H team to distribute care plan Yes ☐ No ☐

Signature of Hospital2Home team member completing form.....

Name and designation.....

Date and time.....

Care plan to be faxed to all professionals attending the case conference. The original document form to be filed in the patient's medical notes at The Royal Brompton NHS Foundation Trust.

Appendix C2c Post case conference follow up

Participant id.....

Royal Brompton & Harefield 
NHS Foundation Trust

Date of Case Conference __ / __ / __

Hospital2Home

Post Case Conference Follow Up

Follow up	Date Due	Date completed	Initials
2 week			
1 month			
2 month			
Date & place of death			

Version 1.0 27/02/11

Participant id

Follow up to nominated key worker at two weeks post case conference

Date ____ / ____ / ____

Palliative Performance Scale					
%	Ambulation	Activity and evidence of disease	Self-care	Intake	Level of consciousness
100	Full	Normal activity No evidence of disease	Full	Normal	Full
90	Full	Normal activity Some evidence of disease	Full	Normal	Full
80	Full	Normal activity with effort Some evidence of disease	Full	Normal or reduced	Full
70	Reduced	Unable to do normal job/work Some evidence of disease	Full	Normal or reduced	Full
60	Reduced	Unable to do hobby/house work Significant disease	Occasional assistance necessary	Normal or reduced	Full or confusion
50	Mainly sit/lie	Unable to do any work Extensive disease	Considerable assistance required	Normal or reduced	Full or confusion
40	Mainly in bed	As above	Mainly assistance	Normal or reduced	Full or drowsy or confusion
30	Totally bed bound	As above	Total care	Reduced	Full or drowsy or confusion
20	As above	As above	Total care	Minimal sips	Full or drowsy or confusion
10	As above	As above	Total care	Mouth care only	Drowsy or coma
0	Death	-	-	-	-

Notes/issues

Details of any hospital readmissions

Participant id

Follow up to nominated key worker at one month post case conference

Date ____ / ____ / ____

Palliative Performance Scale					
%	Ambulation	Activity and evidence of disease	Self-care	Intake	Level of consciousness
100	Full	Normal activity No evidence of disease	Full	Normal	Full
90	Full	Normal activity Some evidence of disease	Full	Normal	Full
80	Full	Normal activity with effort Some evidence of disease	Full	Normal or reduced	Full
70	Reduced	Unable to do normal job/work Some evidence of disease	Full	Normal or reduced	Full
60	Reduced	Unable to do hobby/house work Significant disease	Occasional assistance necessary	Normal or reduced	Full or confusion
50	Mainly sit/lie	Unable to do any work Extensive disease	Considerable assistance required	Normal or reduced	Full or confusion
40	Mainly in bed	As above	Mainly assistance	Normal or reduced	Full or drowsy or confusion
30	Totally bed bound	As above	Total care	Reduced	Full or drowsy or confusion
20	As above	As above	Total care	Minimal sips	Full or drowsy or confusion
10	As above	As above	Total care	Mouth care only	Drowsy or coma
0	Death	-	-	-	-

Notes/issues

Details of any hospital readmissions

Participant id

NHS Foundation Trust

Follow up to nominated key worker at two months post case conference

Date ____ / ____ / ____

Palliative Performance Scale					
%	Ambulation	Activity and evidence of disease	Self-care	Intake	Level of consciousness
100	Full	Normal activity No evidence of disease	Full	Normal	Full
90	Full	Normal activity Some evidence of disease	Full	Normal	Full
80	Full	Normal activity with effort Some evidence of disease	Full	Normal or reduced	Full
70	Reduced	Unable to do normal job/work Some evidence of disease	Full	Normal or reduced	Full
60	Reduced	Unable to do hobby/house work Significant disease	Occasional assistance necessary	Normal or reduced	Full or confusion
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30	Totally bed bound	As above	Total care	Reduced	Full or drowsy or confusion
20	As above	As above	Total care	Minimal sips	Full or drowsy or confusion
10	As above	As above	Total care	Mouth care only	Drowsy or coma
0	Death	-	-	-	-

Notes/issues

Details of any hospital readmissions

NHS Foundation Trust

Include

Name (block capitals):

Name (block capitals):

Designation:.....

Designation:.....

Signature:

Signature:

Date and time:

Date and time:

Appendix C2d H2H patient list

Hospital2Home Research study – Patient List Instructions for On-call staff

The patients listed below are part of the Hospital2Home Research study. In the event of them contacting the Trust to discuss treatment issues, symptom management or admission then please refer to the entries on the EPR made by the Hospital2Home team and contact Donna Louise Laird (H2H nurse) on 07968269158 during working hours. Out of hours please contact the on-call Palliative Care Consultant via switchboard.

Name of patient	Hospital number	Diagnosis	Date discharged	Date of last H2H EPR entry

Appendix C2e Preferred priorities of care document

Participant id.....

Preferred Priorities of Care Document

The aim of advance care planning is to develop better communication and recording of patient wishes. This should support planning and provision of care based on the needs and preferences of patients and their carers. This Preferred Priorities of Care document should be used as a guide, to record what the patient DOES WISH to happen, to inform planning of care.

This is different to a legally binding refusal of specific treatments, or what a patient DOES NOT wish to happen, as in an Advanced Decision or Living Will.

Ideally the process of ascertaining a patient's Preferred Priorities of Care should inform future care from an early stage. Due to the sensitivity of some of the questions, some patients may not wish to answer them all, or to review and reconsider their decisions later. This is a 'dynamic' planning document to be reviewed as needed and can be in addition to an Advanced Decision document that a patient may have agreed.

Patient Name:	Consultant/Team Details:
Address:	
DOB: Hosp no:	Date commenced:
Name of family members involved in discussions:	
Contact tel:	
Name of healthcare professional involved in discussions:	
Role:	
Contact tel:	
Date and time:	

Participant id.....

NHS Foundation Trust

Thinking ahead to the future

What elements of care are important to you and what would you like to happen?

What would you **NOT** want to happen?

NHS Foundation Trust

<p>Do you have a Living Will or Legal Advanced Decision document? Yes /No</p> <p>If yes please give details (who has a copy?)</p>		
<p>Proxy / next of kin Who else would you like to be involved if it ever becomes difficult to make decisions? Do they have Lasting Power of Attorney (LPA)?</p> <p>Contact 1 Tel..... LPA Yes / No</p> <p>Contact 2 Tel..... LPA Yes / No</p>		
<p>Preferred place of care If your condition deteriorates where would you most like to be cared for?</p> <p>1st choice</p> <p>2nd choice</p> <p>Comments</p>		
<p>Preferred place of death Have you had any thoughts about where you might prefer to die should your condition deteriorate?</p> <p>1st choice</p> <p>2nd choice</p> <p>Comments</p>		
<p>Do you have any special requests or preferences?</p>		
<p>Do you have any comments or wishes that you would like to share with others?</p>		

Participant id.....

NHS Foundation Trust

Record of discussions/annotations and professional involved

Section of document completed / amended	Action taken	Outcome
<p>Date/Time:.....</p> <p>Signature:.....</p> <p>Print Name:.....</p> <p>Job Title:.....</p>		

Section of document completed amended	Action taken	Outcome
<p>Date/Time:.....</p> <p>Signature:.....</p> <p>Print Name:.....</p> <p>Job Title:.....</p>		

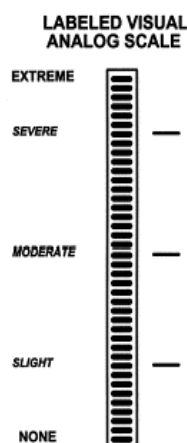
Section of document completed amended	Action taken	Outcome
<p>Date/Time:.....</p> <p>Signature:.....</p> <p>Print Name:.....</p> <p>Job Title:.....</p>		

Appendix C3 Outcome measures

Outcome measures

POS (see appendix 11)

VAS for breathlessness



D-12:

Participants complete the D-12 in reference to their experience of breathlessness “these days” at baseline and follow-up. D-12 consists of 12 descriptor items on a scale of none (0), mild (1), moderate (2), or severe (3). It provides an overall score for breathlessness severity that incorporates seven physical items and five affective items. The time reference period for “these days” captures the current level of breathlessness experienced by patients as opposed to specifically on the day of the test or in response to a specific activity. Total scores from the D-12 range from 0 to 36, with higher scores corresponding to greater severity.

McGILL QUALITY OF LIFE QUESTIONNAIRE

Instructions

The questions in this questionnaire begin with a statement followed by two opposite answers. Numbers extend from one extreme answer to its opposite.

Please circle the number between 0 and 10 which is most true for you.

There are no right or wrong answers.

Completely honest answers will be most helpful

EXAMPLE

I am hungry:

not at all 0 1 2 3 4 5 6 7 8 9 10 **extremely**

- If you are not even a little bit hungry, you would circle 0
- If you are a little hungry (you just finished a meal but still have room for dessert), you might circle a 1, 2 or 3
- If you are feeling moderately hungry (because mealtime is approaching), you might circle a 4, 5 or 6
- If you are very hungry (because you haven't eaten all day), you might circle a 7, 8 or 9
- If you are extremely hungry, you would circle 10.

BEGIN HERE:

IT IS VERY IMPORTANT THAT YOU ANSWER ALL QUESTIONS FOR HOW YOU HAVE
BEEN FEELING JUST IN THE PAST TWO (2) DAYS

PART A

Considering all parts of my life – physical, emotional, social, spiritual, and financial –*over the past two (2) days* the quality of my life has been:

very bad 0 1 2 3 4 5 6 7 8 9 10 **excellent**

PART B

- (1) For questions in Part 'B', please list the **PHYSICAL SYMPTOMS OR PROBLEMS** which have been the biggest problem for you over the past **two (2)** days. (Some examples are: pain, tiredness, weakness, nausea, vomiting, constipation, diarrhoea, trouble sleeping, shortness of breath, lack of appetite, sweating, immobility. Feel free to refer to others if necessary).
- (2) Circle the number which best shows how big a problem each one has been for you **OVER THE PAST TWO (2) DAYS**.
- (3) If, over the past two (2) days, you had **NO** physical symptoms or problems, or only one or two, answer for each of the ones you have had and write 'none' for the extra questions in Part B, and then continue to Part C.

1. Over the past two (2) days,
one troublesome symptom has been:.....
(write symptom)
- no problem** 0 1 2 3 4 5 6 7 8 9 10 **tremendous problem**
2. Over the past two (2) days,
one troublesome symptom has been:.....
(write symptom)
- no problem** 0 1 2 3 4 5 6 7 8 9 10 **tremendous problem**
3. Over the past two (2) days,
one troublesome symptom has been:.....
(write symptom)
- no problem** 0 1 2 3 4 5 6 7 8 9 10 **tremendous problem**

4. Over the past two (2) days I have felt:

physically 0 1 2 3 4 5 6 7 8 9 10 **physically terrible**
well

PART C

*Please choose the number which best describes your feelings and thoughts
OVER THE PAST TWO (2) DAYS.*

5. Over the past two (2) days, I have been depressed:

not at all 0 1 2 3 4 5 6 7 8 9 10 **extremely**

6. Over the past two (2) days, I have been nervous or worried:

not at all 0 1 2 3 4 5 6 7 8 9 10 **extremely**

7. Over the past two (2) days, how much of the time did you feel sad?

never 0 1 2 3 4 5 6 7 8 9 10 **always**

8. Over the past two (2) days, when I thought of the future, I was:

not afraid 0 1 2 3 4 5 6 7 8 9 10 **terrified**

9. Over the past two (2) days, my life has been:

utterly 0 1 2 3 4 5 6 7 8 9 10 **very**
meaningless **purposeful**
and without **and**
purpose **meaningful**

10. Over the past two (2) days, when I thought about my whole life, I felt that in achieving life goals I have:

made no 0 1 2 3 4 5 6 7 8 9 10 **progressed**
progress **to complete**
whatsoever **fulfillment**

11. Over the past two (2) days, when I thought about my life, I felt that my life to this point has been:

completely 0 1 2 3 4 5 6 7 8 9 10 **very**
worthless **worthwhile**

12. Over the past two (2) days, I have felt that I have:

no control 0 1 2 3 4 5 6 7 8 9 10 **complete**
over my **control over**
life **my life**

13. Over the two (2) days, I felt good about myself as a person

completely 0 1 2 3 4 5 6 7 8 9 10 **completely**
disagree **agree**

14. To me, the past two (2) days were:

a burden 0 1 2 3 4 5 6 7 8 9 10 **a gift**

15. Over the past two (2) days, the world has been:

an 0 1 2 3 4 5 6 7 8 9 10 **caring and**
impersonal **responsive**
unfeeling place **to my needs**

16. Over the past two (2) days, I felt supported:

not at all 0 1 2 3 4 5 6 7 8 9 10 **completely**

PART D

Please list or describe the things which had the greatest effect on your quality of life in the past two (2) days. Please tell us whether each thing you list made your quality of life better or worse during this time. If you need more space, please continue on the back of this page.

Palliative Performance Status (PPS) Scale

The purpose of the Palliative Performance Scale (PPS) is to assess the physical condition and functional status of persons receiving palliative care. Scores may range from 0 (dead) to 100 (normal functioning). The PPS measures three broad areas of function: intake, level of consciousness, and mobility. The PPS is scored from 0–100% at 10% increments. The PPS level for a given patient is determined by reading across the table at each 10% decrement to find the overall best fit. 'Stronger' performance factors are noted to be located on the left of the instrument 'softer' ones on the right. Patients who have a lower PPS generally are more functionally impaired than those with higher scores. Prognosis is generally related to functional status in most palliative care patients.

%	Ambulation	Activity and evidence of disease	Self-care	Intake	Level of consciousness
100	Full	Normal activity No evidence of disease	Full	Normal	Full
90	Full	Normal activity Some evidence of disease	Full	Normal	Full
80	Full	Normal activity with effort Some evidence of disease	Full	Normal or reduced	Full
70	Reduced	Unable to do normal job/work Some evidence of disease	Full	Normal or reduced	Full
60	Reduced	Unable to do hobby/house work Significant disease	Occasional assistance	Normal or reduced	Full or confusion
50	Mainly sit/lie	Unable to do any work Extensive disease	Considerable assistance	Normal or reduced	Full or confusion
40	Mainly in bed	As above	Mainly assistance	Normal or reduced	Full or drowsy or confusion
30	Bed bound	As above	Total care	Reduced	Full or drowsy or confusion
20	As above	As above	Total care	Sips	Full or drowsy or confusion
10	As above	As above	Total care	Mouth care	Drowsy or coma
0	Death	-	-	-	-

Medical Research Council Dyspnea Scale:

Medical Research Council (MRC) dyspnea scale (score range, 1-5, with higher scores indicating greater impairment) will be used to classify participants according to activity limitation.

The MRC Breathlessness Scale

Grade	Degree of breathlessness related to activities
1	Not troubled by breathlessness except on strenuous exercise
2	Short of breath when hurrying on the level or walking up a slight hill
3	Walks slower than most people on the level, stops after a mile or so, or stops after 15 minutes walking at own pace
4	Stops for breath after walking about 100 yds or after a few minutes on level ground
5	Too breathless to leave the house, or breathless when undressing

Hospital Anxiety and Depression Scale:

The 14-item Hospital Anxiety and Depression Scale (HADS) is a validated and widely used tool for assessing psychological distress. The HADS comprises seven items that tap anxiety (score range, 0-21) and seven items that tap depression (score range, 0-21), with higher scores corresponding to greater distress.

Hospital Anxiety and Depression Scale (HADS)

Patients are asked to choose one response from the four given for each interview. They should give an immediate response and be dissuaded from thinking too long about their answers. The questions relating to anxiety are marked "A", and to depression "D". The score for each answer is given in the right column. Instruct the patient to answer how it currently describes their feelings.

A	I feel tense or 'wound up':	
	Most of the time	3
	A lot of the time	2
	From time to time, occasionally	1
	Not at all	0

D	I still enjoy the things I used to enjoy:	
	Definitely as much	0
	Not quite so much	1
	Only a little	2
	Hardly at all	3

A	I get a sort of frightened feeling as if something awful is about to happen:	
	Very definitely and quite badly	3
	Yes, but not too badly	2
	A little, but it doesn't worry me	1
	Not at all	0

D	I can laugh and see the funny side of things:	
	As much as I always could	0
	Not quite so much now	1
	Definitely not so much now	2
	Not at all	3

A	Worrying thoughts go through my mind:	
	A great deal of the time	3
	A lot of the time	2
	From time to time, but not too often	1
	Only occasionally	0

D	I feel cheerful:	
	Not at all	3
	Not often	2
	Sometimes	1
	Most of the time	0

A	I can sit at ease and feel	
---	-----------------------------------	--

	relaxed:	
	Definitely	0
	Usually	1
	Not Often	2
	Not at all	3

D	I feel as if I am slowed down:	
	Nearly all the time	3
	Very often	2
	Sometimes	1
	Not at all	0

A	I get a sort of frightened feeling like 'butterflies' in the stomach:	
	Not at all	0
	Occasionally	1
	Quite Often	2
	Very Often	3

D	I have lost interest in my appearance:	
	Definitely	3
	I don't take as much care as I should	2
	I may not take quite as much care	1
	I take just as much care as ever	0

A	I feel restless as I have to	
---	-------------------------------------	--

	be on the move:	
	Very much indeed	3
	Quite a lot	2
	Not very much	1
	Not at all	0

D	I look forward with enjoyment to things:	
	As much as I ever did	0
	Rather less than I used to	1
	Definitely less than I used to	2
	Hardly at all	3

A	I get sudden feelings of panic:	
	Very often indeed	3
	Quite often	2
	Not very often	1
	Not at all	0

D	I can enjoy a good book or radio or TV program:	
	Often	0
	Sometimes	1
	Not often	2
	Very seldom	3

	Scoring (add the As = Anxiety. Add the Ds = Depression). The norms below will give you an idea of the level of Anxiety and Depression.	
	0-7 = Normal	
	8-10 = Borderline abnormal	
	11-21 = Abnormal	

Caregiver Quality of Life

There is no current tool in non-malignant respiratory disease. Therefore this tool will be used which has been validated in cancer patients. It will be made clear to the informal caregiver that the patient does not have cancer.

CAREGIVER QUALITY OF LIFE- CANCER

Below is a list of statements that other people caring for loved ones with cancer have said are important. By circling one number per line, please indicate how true each statement has been for you during the past 7 days.

0	-	Not at all	2	-	Somewhat
1	-	A little bit	3	-	Quite a bit
		4	=		Very much

During the past 7 days:

1.	It bothers me that my daily routine is altered.	0	1	2	3	4
2.	My sleep is less restful.	0	1	2	3	4
3.	My daily life is imposed upon.	0	1	2	3	4
4.	I am satisfied with my sex life.	0	1	2	3	4
5.	It is a challenge to maintain my outside interests.	0	1	2	3	4
6.	I am under a financial strain.	0	1	2	3	4
7.	I am concerned about our insurance coverage.	0	1	2	3	4
8.	My economic future is uncertain.	0	1	2	3	4
9.	I fear my loved one will die.	0	1	2	3	4
10.	I have more of a positive outlook on life since my loved one's illness.	0	1	2	3	4
11.	My level of stress and worries has increased.	0	1	2	3	4
12.	My sense of spirituality has increased.	0	1	2	3	4
13.	It bothers me, limiting my focus to day to day.	0	1	2	3	4
14.	I feel sad.	0	1	2	3	4
15.	I feel under increased mental strain.	0	1	2	3	4
16.	I get support from my friends and neighbors.	0	1	2	3	4
17.	I feel guilty.	0	1	2	3	4
18.	I feel frustrated.	0	1	2	3	4

Zarit Burden Inventory

Multidimensional measures of caregiver burden give a sensitive reading of caregivers' feelings and a sophisticated picture of caregivers' responses to the demands of care. However, there are no validated measures in ILD. A measure which has been widely used in Alzheimers is being used.

THE ZARIT BURDEN INVENTORY

Please circle the response the best describes how you feel. Never	Rarely	Sometimes	Quite Frequently	Nearly Always	Score
1. Do you feel that your relative asks for more help than he/she needs?	0	1	2	3	4
2. Do you feel that because of the time you spend with your relative that you don't have enough time for yourself?	0	1	2	3	4
3. Do you feel stressed between caring for your relative and trying to meet other responsibilities for your family or work?	0	1	2	3	4
4. Do you feel embarrassed over your relative's behaviour?	0	1	2	3	4
5. Do you feel angry when you are around your relative?	0	1	2	3	4
6. Do you feel that your relative currently affects our relationships with other family members or friends in a negative way?	0	1	2	3	4
7. Are you afraid what the future holds for your relative?	0	1	2	3	4
8. Do you feel your relative is dependent on you?	0	1	2	3	4
9. Do you feel strained when you are around your relative?	0	1	2	3	4
10. Do you feel your health has suffered because of your involvement with your relative?	0	1	2	3	4
11. Do you feel that you don't have as much privacy as you would like because of your relative?	0	1	2	3	4
12. Do you feel that your social life has suffered because you are caring for your relative?	0	1	2	3	4
13. Do you feel uncomfortable about having friends over because of your relative?	0	1	2	3	4

14. Do you feel that your relative seems to expect you to take care of him/her as if you were the only one he/she could depend on?	0	1	2	3	4	
15. Do you feel that you don't have enough money to take care of your relative in addition to the rest of your expenses?	0	1	2	3	4	
16. Do you feel that you will be unable to take care of your relative much longer?	0	1	2	3	4	
17. Do you feel you have lost control of your life since your relative's illness?	0	1	2	3	4	
18. Do you wish you could leave the care of your relative to someone else?	0	1	2	3	4	
19. Do you feel uncertain about what to do about your relative?	0	1	2	3	4	
20. Do you feel you should be doing more for your relative?	0	1	2	3	4	
21. Do you feel you could do a better job in caring for your relative?	0	1	2	3	4	
22. Overall, how burdened do you feel in caring for your relative?	0	1	2	3	4	
Total Score (out of 88)						

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Interpretation of Score	
0 – 21	little or no burden
21 – 40	mild to moderate burden
41 – 60	moderate to severe burden
61 – 88	severe burden

Score values and interpretation are guidelines only, as discussed in:
 Robert R. Heavey G. and Proville M (2000) *Canadian J Aging* 19: 494-507

Appendix C4 Topic guide for qualitative interviews

TOPIC GUIDE FOR QUALITATIVE INTERVIEW

(to be further developed through RCT)

General Topics to explore:

- *What do you feel are the most important aspects of Hospital2Home (H2H)?*

Prompts will include: evidenced based guidelines, codifying responsibility, multi-professional working, crisis management, advance care planning

- *What have you found particularly helpful?*

Prompts will include: evidenced based guidelines, codifying responsibility, multi-professional working, crisis management, advance care planning

- *Is there anything about the intervention that you found unhelpful?*

- *What if any improvements would you like to see in the H2H model of care?*

Appendix C5 Prognostic tool



THE FLEISCHNER SOCIETY
Annual Meeting Registration
Thursday, June 3 – Sunday, June 6, 2010
Intercontinental Hotel
Cleveland, Ohio USA

**Registration
form due**

May 3, 2010

Submit completed form to:
hwollach@acr-arss.org or
fax: 703 716 4487

Abstract Submission Form

DATE (MM/DD/YYYY):	27 th April 2010
Submitted by:	David M Hansell
Title:	A simple prognostic staging system for idiopathic fibrosing lung disease
Authors:	AU Wells, DM Hansell*, R Barker, A Devaraj, AJ Edey
Affiliations:	Dept of Radiology and Interstitial Lung Disease Unit, Royal Brompton Hospital, London SW3 6NP, UK
Please use the space provided below to complete your abstract. Submissions should not exceed 1 page.	

Background and Aim: For patients with interstitial lung disease, assistance with broad management decisions cannot easily be extracted from studies using continuous variable scores. In a study of systemic sclerosis-related pulmonary fibrosis a dichotomous mild versus extensive staging system has successfully been used to identify clear prognostic differences. The same principles were used in an attempt to construct a staging system for the idiopathic fibrotic interstitial pneumonias, which have a more progressive course than systemic sclerosis-related pulmonary fibrosis.


Materials and Methods: The HRCTs of 146 consecutive patients with a multidisciplinary team diagnosis of fibrotic idiopathic interstitial pneumonia were scored by two observers to the nearest 5% (at 6 levels) for the extent of abnormal lung (with the proportions of HRCT patterns, including honeycombing, also recorded). Pulmonary function tests were tabulated and the composite physiologic index (CPI) was derived using the formula: $92.1 - (0.63 \times \%DLco) - (0.55 \times \%FVC) + (0.34 \times \%FEV1)$. Baseline variables were evaluated against mortality using proportional hazards analysis, with data given as hazards ratios [HR] with confidence intervals [CI] and p values.

Results: Optimal thresholds, best separating bad versus better outcome were: a) CT extent = 50% (HR 3.5 [CI 2.20, 5.4]), b) proportion of honeycombing = 25% (HR 3.0 [CI 1.9, 4.8]), c) CPI level = 50 units (HR 3.3 [CI 2.0, 5.4]), $p < 0.0005$ for all. On multivariate analysis, all three thresholds strongly and independently predicted mortality. Total disease on CT was categorised as limited (< 40%), extensive (> 60%) or indeterminate (40–60%). The proportion of honeycombing was recorded as limited (< 15%), extensive (> 35%) or indeterminate (15–35%). Staging was primarily assigned from the total CT extent of disease, but for indeterminate cases the extent of honeycombing was integrated; when both CT variables were indeterminate a CPI threshold of 50 units was used.

There was striking separation in survival between limited (n=36) and extensive (n=100) disease (HR=5.2 [CI=3.3, 8.1] $p < 0.0005$); the latter group (extensive disease) had a 10% survival at two years.

Conclusion: This simple dichotomous staging system serves to identify a minority of patients for whom proactive planning of end of life care is appropriate.

Appendix C6a Patient information sheet

Royal Brompton & Harefield 

NHS Foundation Trust

Royal Brompton Hospital
Sydney Street
London
SW3 6NP

PATIENT INFORMATION SHEET

A fast-track randomised controlled trial to evaluate a Hospital2Home palliative care service for patients with advanced Progressive Interstitial Fibrotic Interstitial Lung Disease

The H2H PIF-ILD project

Chief / Principal Investigator
Dr Julia Riley
Palliative Care Research Team
Department of Palliative Medicine
Royal Marsden and Royal Brompton NHS Foundation Trusts
Chelsea,
London
SW3 6NP
0207 808 2761

Study Coordinator
Dr Sabrina Bajwah

Invitation paragraph

We would like to invite you to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve for you. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.
Thank you for reading this.

What is the purpose of the study?

This study is trying to find out how doctors and nurses from the hospital can best help GPs and community nurses to care for people with advanced fibrotic interstitial lung disease in their place of choice, which is most commonly home. We are hoping to help improve symptoms, quality of life and stop people being admitted to hospital unnecessarily.

We are studying patients like you who are cared for by the Royal Brompton Hospital.

Currently the Royal Brompton Hospital team keep your GP informed about your care through letters from clinic and discharge summaries without a case conference meeting held in your home.

This study will compare patients who have a case conference meeting immediately and those who receive it after a delay, with the aim of finding the best way hospital teams can keep yourself, your GP and your community nurses informed.

It will also look at your symptoms and experiences in the community, as well as looking at the experiences of your close family and carers. This will allow us to work out the best way to improve the services in the community to support GP's, community nurses, patients and their carers.

Why have I been invited?

You have been invited to take part because you are a patient with advanced fibrotic interstitial lung disease whose focus of care is being transferred from the hospital setting to the community. We are inviting 52 patients like you, along with their close family and carers, to take part in the study.

Do I have to take part?

It is up to you whether or not you take part. If you do not wish to take part in the case conference then you can let any of the team looking after you know at any point in time. If there are certain topics that you do not wish to discuss at the case conference, then if you let a member of the Hospital2Home team know, then these will not be discussed. With your permission these may be discussed separately. If you do not wish to attend the case conference but would still like to go ahead in the study, then you can nominate a loved one/carer to attend the case conference instead. If you decide to take part you will be given this information sheet to keep along with a record of when we will contact you, and you will be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

What will happen to me if I take part?

Initially you and your loved one/carer will undergo a baseline interview with the researcher which will take approximately 30-45 minutes. This will involve completing questionnaires about symptoms, quality of life and the current help you receive.

With your consent, a case conference will be organised in your home (or place of your choice) either immediately or after 4 weeks. You, your loved one/carer, the Hospital2Home specialist nurse, GP, district nurse, social worker and community palliative care nurse (and any other important health professionals involved in your care) are invited to attend. Current and anticipated care needs are discussed, and an action plan is agreed allocating a responsible health care professional for each item. During the case conference, a care plan individual to your needs will be made. This is then communicated with local services and all involved in your care. The aim is to enable improved symptom control, quality of life, crisis prevention and decreased hospital admissions. In addition, you will have the opportunity to ask any questions about your

disease and plan for the future. The Hospital2Home specialist nurse will follow up each case conference (at 2 weeks, 1 month and 2 months) with you and the health professionals involved to ensure quality and control of the care received.

After leaving the hospital and during the next 2 months, you and your loved one/carer will be phoned at home by the researcher to again complete the same questions asked in the first interview. There will be 2 telephone interviews like this (at 4 weeks and 8 weeks after you enter the study) and they will each take about 30 minutes.

Your loved one/carer will be contacted weekly by telephone for 5 minutes to check if you have needed any extra health services or equipment over that week.

If at any point during the study the researcher feels you are too unwell to complete the questionnaires you will not be asked to do so, but your loved one/carer can continue to complete their questionnaires if they so wish.

After the last contact to complete the questionnaires, with your permission the researcher will keep in contact with your GP (who will be informed of your participation in the study) about your health.

In addition, after the 8 week study period, you and your loved one/carer may be asked to take part in a recorded interview with the researcher. This will last approximately 30-40 minutes and we will explore the aspects of the study that you feel have been most important.

What is the intervention being tested?

The Hospital2Home case conference intervention is being tested. This intervention is designed to facilitate the transfer of care from the acute setting to the community setting and to help alleviate the symptoms and improve the quality of life of fibrotic interstitial lung disease patients and their loved ones/carers.

What are the alternatives for diagnosis or treatment?

You do not have to participate in this study. If you do not participate in the study, you will continue to receive normal supportive treatment in the community from your GP and other community health professionals.

What are the possible disadvantages and risks of taking part?

Taking part in the study will not adversely affect any aspect of your treatment at home or in hospital. Sometimes being asked about your feelings may be difficult to answer. If so, you do not have to continue or answer anything you do not feel comfortable with. If you feel after answering our questions you need more support to deal with any emotions you have we will arrange this for you.

Are there any benefits to me if I participate in the study?

You will be offered a referral for additional support and assessment if necessary. The study will help people in the future by making health professionals more aware of the problems or experiences of patients who have fibrotic interstitial lung disease, and their loved ones/carers, who are looked after in the community. This will lead to deciding how support can be organised between the hospital and the community to improve current practice

What happens when the research study stops?

At the end of the research, your care will continue as usual in the community.

What if I do not want to carry on with the study?

You may withdraw from the study at anytime. You may do so without any penalty or loss of benefits to which you are otherwise entitled at this hospital, including the present and future standard of medical care that you receive. If you do not want to take part in this study, you will receive standard care in the community. Should you decide to withdraw from the study for any reason, you are asked to contact Dr Sabrina Bajwah immediately. Should your participation in the study be terminated, regardless of the reason, you will not suffer any penalties or loss of benefits to which you are otherwise entitled.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions:

Dr Sabrina Bajwah
Palliative Care Research Team
Department of Palliative Medicine
Royal Marsden and Royal Brompton NHS Foundation Trusts
Chelsea,
London
0207 808 2761

If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. You can contact the Patient Advice and Liaison Services office at the Royal Brompton Hospital on 020 7349 7715

Harm

If the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for legal action for compensation against the Royal Brompton and Harefield NHS Trust but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you. NHS indemnity does not offer no-fault compensation i.e. for non-negligent harm, and NHS bodies are unable to agree in advance to pay compensation for non-negligent harm.

Will my taking part in the study be kept confidential?

All information which is collected about you during the course of the research will be kept strictly confidential. Any information about you which leaves the hospital will have your name, address and personal details removed so that you cannot be recognised from it. We will request your consent before informing your GP about your participation in the study. If you consent to take part in the research, any of your medical records may be looked at by a member of the research team or regulatory authority. Your name, however, will not be disclosed. You will not be identified in any report or publication that arises as a result of the study.

Will my General Practitioner / Family doctor (GP) be informed of my involvement?

Provided you consent to this, your GP will be informed that you are participating in the study. In addition, after the last contact to complete the questionnaires, the researcher will keep in contact with your GP about your health.

What will happen to the results of the research study?

The results of the study will not be available for about 2 years. The researchers will write a report, which will be publicised at various medical meetings, and in various medical journals. If you would like a summary of the results when available please inform your doctor or research nurse.

Your medical records will be made available for review by the study investigators and regulatory authorities (who periodically check that the studies are being carried out correctly). The information in these records will be kept confidential but on rare occasions the law may require disclosure to third parties. At the end of the project all the research results are gathered together and analysed. The researchers have a professional responsibility to publish their findings, however your identity will not be revealed. Most research is published in the medical press – if you are interested in knowing the overall results of the study, ask the researchers about this. You are entitled to see any results or information about you under the Freedom of Information Act.

Who is organising and funding the research?

The study is being organised by the Department of Palliative Medicine at the Royal Marsden Hospital and Royal Brompton Hospital. The study is funded by the Royal Marsden and Royal Brompton Palliative Care Research Fund. The researchers will not be paid for including you in the study.

Who has reviewed the study?

All research in the NHS is looked at by an Independent group of people, called a Research Ethics Committee to protect your safety, rights, wellbeing and dignity. This study has been reviewed and given favourable opinion by <enter name of REC>. In addition approval has been gained from local R&D Offices.

Contact for Further Information

If you would like any further information about the study, either now or at time during the course of the study, please ask a member of the Research Team at:

Palliative Care Research Team
Department of Palliative Medicine,
Royal Marsden and Royal Brompton NHS Foundation Trusts,
Chelsea,
London
0207 808 2761

Thank you for taking the time to consider this study. If you do choose to participate, you will be given a copy of this information sheet to keep and also a copy of the consent form that you will be asked to sign.

Carer information sheet

The H2H PIF-ILD project

(A fast-track randomised controlled trial to evaluate a Hospital2Home palliative care service for patients with advanced Progressive Interstitial Fibrotic Interstitial Lung Disease)

'We would like to invite you to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve.'

*Please take time to read the following information carefully and discuss it with friends, relatives and your doctor if you wish. Please ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.
Thank you for reading this'*

What is the purpose of the study?

This study is trying to find out how doctors and nurses from the hospital can best help GPs and community nurses to care for people with lung disease in the patient's place of choice, which is most commonly home. We are hoping to help improve symptoms, quality of life and stop people being admitted to hospital unnecessarily.

We are studying patients with this disease and their loved ones/carers who are cared for by the Royal Brompton Hospital. Currently if your loved one is a patient at the Royal Brompton Hospital the hospital team will keep the GP informed about care through letters from clinic and discharge summaries without a case conference meeting held in their home.

This study will compare patients randomly allocated to have a case conference meeting immediately, or to have a case conference meeting after four weeks with the aim of finding the best way hospital teams can keep yourself, your loved one, the GP and the community nurses informed.

It will also look at your loved one's symptoms and experiences in the community, as well as looking at your experiences. This will allow us to work out the best way to improve the services in the community to support GP's, community nurses, patients and their carers.

Why have I been chosen?

You have been invited to take part because you are the close loved one/carer of a patient with advanced fibrotic interstitial lung disease whose focus of care is being transferred from the hospital setting to the community. We are inviting 52 patients along with their carers like you, to take part in the study.

What will happen to me if I do not take part?

It is up to you whether or not you take part. If you do not take part you will receive standard care (GP and other community support as appropriate), it will not affect the care you or your loved one receives. If you decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care your loved one receives.

What will happen to me if I take part?

Initially you and your loved one will undergo a baseline interview with the researcher which will take approximately 30-45 minutes. This will involve completely questionnaires about symptoms, quality of life and the current help you receive.

With your loved one's consent, a case conference will be organised in their home (or place of their choice) either immediately or after 4 weeks. You, your loved one, the Hospital2Home specialist nurse, GP, district nurse, social worker and community palliative care nurse are invited to attend. Current and anticipated care needs are discussed, and an action plan is agreed allocating a responsible health care professional for each item. During the case conference, a care plan individual to your loved one's needs will be made. This is then communicated with local services, and all involved in their care. The aim is to enable improved symptom control, quality of life, crisis prevention and decreased hospital admissions. In addition, you will have the opportunity to ask any questions about the disease and plan for the future. The Hospital2Home specialist nurse will follow up each case conference (at 2 weeks, 1 month and 2 months) with the health professionals involved to ensure quality and control of the care received.

During the next 2 months, you and your loved one will be phoned at home by the researcher to again complete the same questions asked in the first interview. There will be 2 telephone interviews like this (at 4 weeks and 8 weeks after you enter the study) and they will each take about 30 minutes.

In addition, you will be contacted weekly by telephone for 5 minutes to check if your loved one has needed any extra health services or equipment over that week.

If at any point during the study the researcher feels your loved one is too unwell to complete the questionnaires they will not be asked to do so, but you can continue to complete the questionnaires if you so wish.

After the last contact to complete the questionnaires, the researcher will keep in contact with the general practitioner (who will be informed of participation in the study) about your loved one's health.

In addition, after the 8 week study period, you or your loved one may be asked to take part in a recorded interview with the researcher. This will last approximately 30-40 minutes and we will explore the aspects of the study that you feel have been most important.

What are the possible disadvantages of taking part?

Taking part in the study will not adversely affect any aspect of your loved one's treatment at home or in hospital. Sometimes being asked about your feelings may be difficult to answer. If so, you do not have to continue or answer anything you do not feel comfortable with. If you feel after answering our questions you need more support to deal with any emotions you have we will arrange this for you.

What are the possible benefits of taking part?

You will be offered a referral for additional support and assessment if necessary. The study will help people in the future by making health professionals more aware of the problems or experiences of patients who have fibrotic interstitial lung disease, and their carers, and how they are looked after in the community. This will lead to deciding how support can be organised between the hospital and the community to improve current practice

Will my taking part in this study be kept confidential?

If you consent to take part in the research, any of your research records may be looked at by a member of the research team or regulatory authority. Your name, however, will not be disclosed. You will not be identified in any report or publication that arises as a result of the study.

What will happen to the results of the research study?

The results of the study will not be available for about 2 years. The researchers will write a report, which will be publicised at various medical meetings, and in various medical journals. If you would like a summary of the results when available please inform your doctor or research nurse.

Who is organising and funding the research?

The study is being organised by the Department of Palliative Medicine at the Royal Marsden Hospital and Royal Brompton Hospital. The study is funded by the Royal Marsden and Royal Brompton Palliative Care Research Fund. The researchers will not be paid for including you in the study.

Who has reviewed the study?

The Royal Marsden Hospital/ Institute of Cancer Research's Research and Local Ethics Committee have reviewed the study and have given their approval

Contact for further information:

If you would like further information about the study, then please contact the researchers (see below)

Thank you for reading this information sheet, and for considering taking part in this research.

**Dr Julia Riley and Dr Sabrina Bajwah
Palliative Care Research Team
Department of Palliative Medicine
Royal Marsden NHS Foundation Trust
Chelsea,
London
0207 808 2761**

If you have any questions about whether to participate in the study and wish to seek independent advice then you can contact the Royal Brompton Hospital Patient Advisory Service (PALS). They can be contacted through the switchboard on 0207 352 8121

Appendix C7a Patient consent form

Patient Consent Form

Participant Identification for this trial:

The H2H PIF-ILD project

(A fast-track randomised controlled trial to evaluate a Hospital2Home palliative care service for patients with advanced Progressive Interstitial Fibrotic Interstitial Lung Disease)

1. I confirm that I have read and understand the information sheet dated 2nd June 2011 version 1.2 for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from the research team, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐
4. I understand that my involvement is strictly confidential and no information about me will be used in any way that reveals my identity other than to the researcher(s) ☐
5. I agree to be visited at home by members of the multi-disciplinary team (eg GP, district nurse) for the Hospital2Home case conference intervention ☐
6. I understand that if undertaking the qualitative interview, sections of my interviews will be transcribed and used in publication including academic medical education journals and/or conference presentations and that my anonymity will be preserved. ☐
7. I understand that I can stop the interview at any time if I do not wish to continue the audio recording and that the recording will be erased and the information provided will not be included in the study. ☐
8. I understand that my participation for the qualitative interviews will be audio taped ☐
9. I understand that all data will be anonymised, transferred and held at the Royal Marsden Hospital and treated as strictly confidential and not copied without my permission. Data will be kept in accordance with research governance policies and any raw data on which the results of the project depend will be retained in secure storage in accordance with the Data Protection Act (1998) ☐

Version 1.2 02/06/11

10. I know that my participation should not lead to any potential harm of discomfort and I consent to the processing of my personal information for the purposes of the study

☐

11. I agree that if I become unwell that the data already collected may still be used in the study

☐

I prefer to participate in :

- ☐ Randomised Controlled Trial
- ☐ Individual face to face interview
- ☐ No preference

Name of patient Date Signature

Name of person taking consent Date Signature

Researcher Date Signature

**When completed - 1 for patient;
 1 (original) to be kept in research site file;
 1 for medical notes;
 1 for CRF.**

Would you like a summary sheet of research findings YES/NO

**Dr Julia Riley and Dr Sabrina Bajwah
Palliative Care Research Team
Department of Palliative Medicine
Royal Marsden NHS Foundation Trust
Chelsea,
London
0207 808 2761**

Version 1.2 02/06/11

Appendix C7b Carer consent form

Carer Consent Form

Participant Identification for this trial:

The H2H PIF-ILD project

(A fast-track randomised controlled trial to evaluate a Hospital2Home palliative care service for patients with advanced Progressive Interstitial Fibrotic Interstitial Lung Disease)

1. I confirm that I have read and understand the information sheet dated 27th February 2011 version 1.0 for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand that my involvement is strictly confidential and no information about me will be used in any way that reveals my identity other than to the researcher(s) ☐
4. I understand that if undertaking the qualitative interview, sections of my interviews will be transcribed and used in publication including academic medical education journals and/or conference presentations and that my anonymity will be preserved. ☐
5. I understand that I can stop the interview at any time if I do not wish to continue the audio recording and that the recording will be erased and the information provided will not be included in the study. ☐
6. I understand that my participation for the qualitative interviews will be audio taped ☐
7. I understand that all data will be anonymised, transferred and held at the Royal Marsden Hospital and treated as strictly confidential and not copied without my permission. Data will be kept in accordance with research governance policies and any raw data on which the results of the project depend will be retained in secure storage in accordance with the Data Protection Act (1998) ☐
8. I know that my participation should not lead to any potential harm or discomfort and I consent to the processing of my personal information for the purposes of the study ☐
9. I agree that if I become unwell that the data already collected may still be used in the study ☐

Version 1.1 25/03/11

I prefer to participate in :

- ☐ Randomised Controlled Trial
- ☐ Individual face to face interview
- ☐ No preference

Name of participant Date Signature

Name of person taking consent Date Signature

Researcher Date Signature

**When completed - 1 for participant;
 1 (original) to be kept in research site file;
 1 for CRF.**

Would you like a summary sheet of research findings YES/NO

**Dr Julia Riley and Dr Sabrina Bajwah
Palliative Care Research Team
Department of Palliative Medicine
Royal Marsden NHS Foundation Trust
Chelsea,
London
0207 808 2761**

Version 1.1 25/03/11

Health care professional information sheet

The H2H PIF-ILD project

(A fast-track randomised controlled trial to evaluate a Hospital2Home palliative care service for patients with advanced Progressive Interstitial Fibrotic Interstitial Lung Disease)

Your patient (*insert name and dob*) has agreed to take part in the above research study. Provided below is a brief description of the study and its purpose.

What is the purpose of the study?

Around 500,000 people die in the UK each year. Most people say they would prefer to die at home if given the choice, but 58% die in hospital. This study is trying to find out how doctors and nurses from the hospital can best help GPs and community nurses to care for people in their place of choice and achieve their preferred place of death, and how we can stop people being admitted to hospital unnecessarily. This study will look at people's symptoms and experiences in the community, as well as looking at the experiences of their close family and carers. It will compare a Royal Brompton Hospital case conference based discharge scheme (known as Hospital2Home) with standard care for patients at the Royal Brompton Hospital who do not have a case conference. This will allow us to work out the best way to improve communication between hospital and community health care professionals in order to improve the services in the community to support GP's, community nurses, patients and their carers.

Why has your patient been chosen?

We have invited your patient to take part as they have advanced fibrotic Interstitial Lung Disease and the focus of their care is being transferred back from the Royal Brompton Hospital to the community setting. We are inviting 52 patients in total, along with their close family and carers, to take part in the study.

What will happen to my patient as part of the study?

Your patient will receive the Hospital2Home (H2H) case conference intervention. H2H will be offered in addition to standard services. H2H aims to complement the existing local services and not to duplicate or replace them. This intervention is a new multi-professional, patient centred meeting or case conference that is organised for people nearing the end-of-life. In recent months we have been conducting a review of the literature and interviews of patients, carers and health professionals. This has enabled us to start developing evidenced based guidelines for the management of the physical, psychological, spiritual and end of life-planning needs for these patients. These guidelines will be used in the H2H case conference. The written guidelines will act as a supplement to the actual assessment. With the patients consent, a case conference will be organised in their home (or place of their choice). The patient, carer, H2H CNS, GP, district nurse, social worker and community palliative care nurse are invited to attend. Current and anticipated care needs are discussed, and an action plan is agreed allocating a responsible health care professional for each item. During the case conference, individualised care plans will be made. The

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care plan provides a quality comprehensive Palliative Care assessment. This is then communicated with local services, both primary and specialist teams resulting in streamlining of transfer of data and codifying responsibility for the patient, hospital and community care professionals. The aim is to enable improved symptom control, quality of life, crisis prevention and decreased hospital admissions. In addition, this intervention will aim to manage uncertainty by facilitating early discussion about disease progression, improving communication and addressing end of life planning needs.

The Royal Brompton Marie Curie H2H CNS will deliver teaching on the use of the evidence-based guidelines and will follow up each case conference (at 2 weeks, 1 month and 2 months) to assure quality and control of the care received.

Your patient will be phoned at home by the researcher and be asked some basic questions about their diagnosis and medications, along with a questionnaire about their symptoms and quality of life. They will also be asked about the frequency of home visits from community nurses, carers and yourself, as well as any hospital visits. Their close family member or carer will also be asked some similar questions. We will contact your patient and their carer 3 times over a 2 month period. The first assessment will be a face to face contact (in hospital) and then subsequent contacts may be by telephone at 4 weeks and finally at 2 months. The first visit will take about 45 minutes, and each telephone call after this will take about 30 minutes. The carer or patient will be contacted by telephone weekly for 5 minutes to collate what health services they have used in the previous week.

What are the possible disadvantages of taking part?

Taking part in the study will not adversely affect any aspect of your patient's treatment at home or in hospital.

Your patient or their carer will be offered a referral for additional support and assessment if any new issue is uncovered as part of the research.

What will happen to the results of the research study?

The results of the study will not be available for about 2 years. The researchers will write a report, which will be publicised at various medical meetings, and in various medical journals. If you would like a summary of the results when available please inform a member of the research team.

Who is organising and funding the research?

The study is being organised by the Department of Palliative Medicine at the Royal Marsden and Royal Brompton Hospital. The study is funded by the Royal Marsden and Royal Brompton Palliative Care Research Fund. The researchers will not be paid for including you in the study.

Who has reviewed the study?

The Royal Marsden Hospital/ Institute of Cancer Research's Research and Local Ethics Committee have reviewed the study and have given their approval

Contact for further information:

If you would like further information about the study, then please contact the researchers (see below)

Thank you for reading this information sheet.

Dr Julia Riley
Consultant

Dr Sabrina Bajwah
Research Fellow

Department of Palliative Medicine
Royal Marsden NHS Foundation Trust
Chelsea, London
0207 808 2761

Appendix C9 Marie Curie peer review comments

External referees comment (for applicant)

Applicant: Dr Riley
Attachment No.:
Ref no: 1
Date: MCCC November 2010
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Marie Curie Cancer Care Funding Committee

Referee's Comment on Project Grant Application

In particular we would appreciate your comments on: the importance of the question and its relevance to end of life care research; the originality of the project; the quality of the plan of investigation; the likelihood of its successful conclusion within the time specified; and whether the level of support requested is appropriate.

This page will be fed back to the applicant intact; please do not include any reference to your identity, or any particularly sensitive comments.

Research questions and originality

While many studies during the past years have focused on providing an overview of how care is provided to patients at the end of their lives, there is a consensus in international literature that we need to improve care for all patients. The current study focuses on implementing a care improvement programme and studying the effect on patient and caregiver outcomes.

While the study uses a very specific group of patients to implement its "case conferencing" model, the authors point at the possible applications for other disease groups. It is however not explained why this particular group of patients has been chosen for the intervention or why these patients might benefit the most.

Positive is that the project concerns a next phase in a larger research project in which literature review and earlier work (audit, qualitative work) have already been performed.

However, the international applicability of this H2H programme is not described thoroughly. References to previous papers using case conferencing are limited, and international collaboration concerning this project is not described.

Quality of methodology

- Exploratory trial following the MRC Framework for complex trials seems suitable
- Well worked out methodology
- H2H programme well described. The programme creates the structural conditions for communication.

It would be an additional surplus if the authors would measure differences in communication processes during case conferencing, in an effort to identify the components that work best.

One concern is the number of subjects in the two groups i.e. 25 patients per group. The authors indicate that the research questions are "to assess whether H2H improves symptoms, quality of life, dying at the preferred place" etc and the data analyses include longitudinal analyses, ANCOVA etc. hence, only very large effects of the intervention can be found with such small groups. However, using this limited number of subjects, testing the feasibility of the trial will be possible and inform a possible next main trial.

Likelihood of successful conclusion

The study is embedded into a larger ongoing project – of which part has already been funded by Marie Curie. It also has a clear and realistic planning and is lead by key figures in the palliative care research domain.

Level of support requested

The role of the statistician and health economist is not clear in this project (i.e. the 'phase II trial' part of the whole project).

External referees comment (for applicant)

Applicant: Dr Riley
Attachment No.:
Ref no: 2
Date: MCCC November 2010
For office use only

Marie Curie Cancer Care
Funding Committee

Referee's Comment on Project Grant Application

In particular we would appreciate your comments on: the importance of the question and its relevance to end of life care research; the originality of the project; the quality of the plan of investigation; the likelihood of its successful conclusion within the time specified; and whether the level of support requested is appropriate.

This page will be fed back to the applicant intact; please do not include any reference to your identity, or any particularly sensitive comments.

This ambitious project will be undertaken by a highly qualified team and aims to:
a) evaluate clinical use of a dichotomous staging system to identify patients with Progressive Idiopathic Fibrotic Interstitial Lung Disease for whom proactive planning of EOL care is now appropriate;
b) evaluate evidence-based guidelines for the palliative management of patients with severe PIF-ILD;
c) develop and evaluate a case conference intervention for patients with severe PIF-ILD;
d) assess whether the complex intervention of evidence-based guidelines and case conference affects symptom, QOL caregiver burden and use/costs of formal health and social services and
e) determine whether H2H allows people to achieve their preferred place of death and care.

Mixed method phase II study following previously developed strategy developed in Phase 0+1. Potential benefits to patients, carers and clinical practice are clearly outlined.

While the budget looked appropriate, the health economist is a valuable resource for the team.

The data sharing plan is thorough and comprehensive.

The work being conducted in the theoretical and modelling phases are clearly articulated and provide the matrix for the current application, although I am not certain of the connection between cross cultural needs and PIF-ILD. Descriptions of the setting, recruitment and randomization as well as the intervention were clear and proceeded logically. The POS is a useful and appropriate instrument for measuring primary outcomes in this situation.

Given the prognosis of this illness, I was not clear if the participants will be followed until they die. I wasn't able to locate where this was discussed. The timing of the interviews/data collection was unclear to me from the body of the proposal, although the data analysis section clarified that scores will be compared at 4 and 8 weeks.

Figure 1 is helpful in better understanding the intended design.

External referees comment (for applicant)

Applicant: Dr Riley
Attachment No.:
Ref no: 3
Date: MCCC November 2010
For office use only

Marie Curie Cancer Care
Funding Committee

Referee's Comment on Project Grant Application

In particular we would appreciate your comments on: the importance of the question and its relevance to end of life care research; the originality of the project; the quality of the plan of investigation; the likelihood of its successful conclusion within the time specified; and whether the level of support requested is appropriate.

This page will be fed back to the applicant intact; please do not include any reference to your identity, or any particularly sensitive comments.

This is a well-constructed proposal from a team with exceptional leadership in the field of innovative palliative care. Pulmonary Fibrosis is one of those 'orphan' conditions that falls outside of conventional palliative medicine practice so it's good to see an application that addresses the needs of both patients and families in the late stages of a condition where the symptom burden (both physical and existential distress) will be profound. Moreover the Higginson group has extensive experience of assessment of new models of care and in particular in the application of the 'fast track' RCT to address significant outcomes that can be experienced by all patients within the trials but on differing timelines.

The early phases of the program are "funded and underway"

The format of the main application precludes detailed descriptions of background issues and important elements of the proposal, but having said that, the key elements are all there. Feasibility issues are addressed, as are sampling issues (appropriate to a mixed methods approach). The use of mixed methods is appropriate and the MRC framework for evaluation of complex interventions is one familiar to this team and again entirely appropriate for the proposal. Outcomes are clearly described (and are relevant and easily measured) and analysis is again appropriate to the study design. Recruitment (one per week) may be optimistic but the PI works in a specialized centre where this may be achievable.

Most of the budget items support staff salaries at various FTE levels and seems reasonable. I cannot determine how much overlap there is with a £550,000 donation from the Royal Marsden

Minor comments: The proposed allocation of time to this study by the PI (4 hours per week) seems a tad on the low side but is perhaps a reality if the primary appointment is with a clinical department.

The PI has a relatively limited research CV (7 first author publications), though this is balanced by the more senior members of the team. I saw only one letter of support from colleagues in Respiratory Medicine and would have expected more.

SUMMARY: I would be confident that this group can complete the study in the timeline proposed and that this study has the potential to serve as a model of the management of late stages of other chronic respiratory illness where continuity across care transitions is meagre at best and often lacking entirely in some locations.

Appendix C10 Answers to peer reviewers' comments



The Royal Marsden **NHS**
NHS Foundation Trust

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SW3 6JJ
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Direct Dial: 0207 808 2761

Answers to Marie Curie peer review comments

21/10/10

Dear Sir,

Re: Developing and evaluating a Hospital2Home palliative care service for patients with severe idiopathic fibrotic Interstitial Lung Disease: Phase II

Please see below our answers to referees comments.

Referee 1

1. Why this group of patients have been chosen and will benefit from the intervention most.

PIF-ILD patients have a high symptom burden and poor quality of life whilst dying from their disease.¹⁻⁵ Our own audit showed limited palliative care involvement in the last year of life and death occurring in hospital in the majority of patients. RBH figures for 2009 show that 154 patients had 325 admissions (63 had multiple admissions), total number of inpatient days 1,674.

Previous uncertainty about prognosis has hindered planning for end-of-life needs in non-malignant disease. The prognostic tool developed by Wells allows prognostication and identification of patients with PIF-ILD who are likely to die <1 year.(Appendix 5) This tool is unique in non-malignant disease and makes this group of patients ideal to study this model of care in.



Chairman: Mrs Tessa Green
Chief Executive: Miss Cally Palmer CBE
www.royalmarsden.nhs.uk

2. International applicability of H2H

Abernethy et al conducted a RCT showing that case conferencing improved functional performance, decreased hospital admissions, enhanced coordination of care and improved resource utilisation.⁶

A pilot study at the Royal Marsden Hospital (RMH) has used a H2H model (tailored to cancer patients). 133 patients received H2H, and 121 patients died- 80% in their preferred place (home or hospice). Further evaluation of effectiveness and cost is now being conducted. There has been no research into using this model in non-malignant disease. This research gives the opportunity to use a RCT to evaluate this model of care.

Riley has communicated with Currow's team⁶ in developing the H2H model and has used their work to inform application of the model to the UK.

The next stage of our research will be to conduct a phase III multi-centre, national trial. In the long term, we will aim for international collaboration in other countries. The model will be tailored to the structure of each healthcare system.

3. Measuring differences in communication processes during case conferencing

The phase II RCT is a mixed methods study and includes qualitative interviews of patients, carers and health professionals who have been involved in H2H. This will allow us to explore the aspects and components of the communication process that participants have found most helpful. Specific tools to measure differences in communication processes will be considered for future work in phase III.

4. Number of subjects

Based on clinical and research experience and data published from other studies⁷ a sample of 25 patients in each group would enable us to detect clinically significant differences of >1.6 on the POS (for individual items), where items had a standard deviation of <2, at $p < 0.05$, power 80%. Based on the local patient numbers (RBH has 500 new referrals yearly for ILD patients) of people with a 30% survival at one year, we estimate to identify 2 patients per week (advice taken from ILD respiratory Consultants Prof Wells and Dr Toby Maher) with 50% recruitment. Recruitment over 1 year would give us 50–52 patients, giving sufficient indication of whether differences between groups were emerging.

Trends in quantitative data will be enforced by the qualitative work. Phase II would then provide the data, at this time lacking, to inform the power calculations for a Phase III RCT.

5. Role of statistician and health economist

The statistician and health economist will be involved in the phase II part of the project. Statistical support for Phase 0&I of the project has been provided by the Project Advisory Group.

Reviewer 2

6. Connection between cross cultural needs and PIF-ILD.

At Kings, Koffman ⁸ has recognised differing palliative care needs and preferences related to ethnicity. Further work is ongoing in other non-malignant diseases (multiple sclerosis). In developing our complex intervention, we wanted to ensure that our preliminary work (phase 0&I) was conducted across different socioeconomic and ethnic groups. In doing so, we hope our intervention will meet the palliative care needs of patients regardless of ethnicity and socioeconomic group making our intervention generalisable nationally and internationally.

7. Follow up.

The H2H intervention will either be received immediately after randomisation or after a 4 week wait. Outcome and cost data is collected at baseline (before randomisation) and 4, 8 weeks. Patients will be followed up until death, documenting achievement of preferred place of care and death. The main text of the proposal has been adapted to make this clearer.

Reviewer 3

8. Recruitment.

Please see point 4 above

9. Overlap of money with £550,000 from RMH H2H money

There is no overlap with the £550,000 awarded to Riley by the RMH, which funded the pilot project referred to in point 2 above. The RMH H2H project has provided background for this project and ongoing economic evaluation will help inform this current project.

10. Experience of PI

Riley has spearheaded the development of the H2H work in the cancer group (she is PI on the H2H cancer project). In addition, she has collaborated closely with the Australian team whilst recognising the changes that need to be developed for transfer to a UK setting. Riley has built collaboration with other departments (King's Department of Palliative Care and Policy and the National Heart and Lung Institute) in developing and taking this project further. The involvement of the other senior researchers alongside Riley will allow full maximisation of this project's potential.

11. Time allocated for project by PI

The PI has significant clinical commitments, this is a necessity. The time allocated to this project will be ring fenced. The research fellow will be adequately supported by all co-investigators and will also have the support of the Cicely Saunders Palliative Care Institute where she will be on a daily basis.

12. Letters of support

Wells (co-investigator) is the lead respiratory clinician for ILD at RBH and has been integral to the design and progress to date of phase 0&I. In addition to the previous letter from Dr Birring (lead ILD consultant at King's College Hospital), we have now attached letters from Dr Maher, Consultant Respiratory Medicine, RBH (Appendix D) and Lucy Pigram, ILD Specialist Sister, RBH (Appendix E).

We continue to remain very committed to taking this project forward.

Please do not hesitate to contact us if you require any further information.



Dr Julia Riley

Head of Department

Royal Marsden & Royal Brompton Palliative Care Service

The Royal Marsden NHS Foundation Trust

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Appendix C11 Adapted POS

Palliative Care Outcome Scale- applicable symptom prompts have been added to question 2

Patient's Questionnaire POS

Please answer the following questions by ticking the box next to the answer that is most true for you. Your answers will help us to keep improving your care and the care of others.

Thank you.

1 Over the past 3 days, have you been affected by pain?

- ☐ 0 Not at all, no effect
- ☐ 1 Slightly – but not bothered to be rid of it
- ☐ 2 Moderately – pain limits some activity
- ☐ 3 Severely – activities or concentration markedly affected
- ☐ 4 Overwhelmingly – unable to think of anything else

2 Over the past 3 days, have other symptoms e.g. having a cough, shortness of breath, fatigue or insomnia been affecting how you feel?

- ☐ 0 No, not at all
- ☐ 1 Slightly
- ☐ 2 Moderately
- ☐ 3 Severely
- ☐ 4 Overwhelmingly

3 Over the past 3 days, have you been feeling anxious or worried about your illness or treatment?

- ☐ 0 No, not at all
- ☐ 1 Occasionally
- ☐ 2 Sometimes – affects my concentration now and then
- ☐ 3 Most of the time – often affects my concentration
- ☐ 4 Can't think of anything else - completely pre-occupied by worry and anxiety

4 Over the past 3 days, have any of your family or friends been anxious or worried about you?

- ☐ 0 No, not at all
- ☐ 1 Occasionally
- ☐ 2 Sometimes – it seems to affect their concentration
- ☐ 3 Most of the time
- ☐ 4 Yes, always preoccupied with worry about me

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5 Over the past 3 days, how much information have you and your family or friends been given?

- ☐ 0 Full information – always feel free to ask what I want
- ☐ 1 Information given but hard to understand
- ☐ 2 Information given on request but would have liked more
- ☐ 3 Very little given and some questions were avoided
- ☐ 4 None at all

6 Over the past 3 days, have you been able to share how you are feeling with your family or friends?

- ☐ 0 Yes, as much as I wanted to
- ☐ 1 Most of the time
- ☐ 2 Sometimes
- ☐ 3 Occasionally
- ☐ 4 Not at all with anyone

7 Over the past 3 days, have you been feeling depressed?

- ☐ 0 No, not at all
- ☐ 1 Occasionally
- ☐ 2 Sometimes
- ☐ 3 Most of the time
- ☐ 4 Yes, definitely

If you have placed a tick in boxes 3 or 4 for this question, please speak with your nurse or doctor at your next appointment.

8 Over the past 3 days, have you felt good about yourself as a person?

- ☐ 0 Yes, all the time
- ☐ 1 Most of the time
- ☐ 2 Sometimes
- ☐ 3 Occasionally
- ☐ 4 No, not at all

9 Over the past 3 days, how much time do you feel has been wasted on appointments relating to your healthcare, e.g. waiting around for transport or repeating tests?

- ☐ 0 None at all
- ☐ 2 Up to half a day wasted
- ☐ 4 More than half a day wasted

10 Over the past 3 days, have any practical matters resulting from your illness, either financial or personal, been addressed?

- ☐ 0 Practical problems have been addressed and my affairs are as up to date as I would wish
- ☐ 2 Practical problems are in the process of being addressed
- ☐ 4 Practical problems exist which were not addressed
- ☐ 0 I have had no practical problems

11 If any, what have been your main problems in the last 3 days?

1

.....

2

.....

12 How did you complete this questionnaire?

- ☐ 0 On my own
- ☐ 1 With the help of a friend or relative
- ☐ 2 With help from a member of staff

Carer's Questionnaire POS

Please answer the following questions by circling the answer, which you think most accurately, describes how the person you care for has been feeling.

1. Over the past 3 days, has s/he been affected by pain?

Not at all, no effect	0
Slightly - but not bothered to be rid of it	1
Moderately - pain limits some activity	2
Severely - activities or concentration markedly affected	3
Overwhelmingly - unable to think of anything else	4

2. Over the past 3 days, have other symptoms e.g. having a cough, shortness of breath, fatigue or insomnia seemed to be affecting how s/he feels?

No, not at all	0
Slightly	1
Moderately	2
Severely	3
Overwhelmingly	4

3. Over the past 3 days, has s/he been feeling anxious or worried about their illness or treatment?

No, not at all	0
Occasionally	1
Sometimes - affects their concentration now and then	2
Most of the time - often affects their concentration	3
Patient does not seem to think of anything else - completely pre-occupied by worry and anxiety	4

4. Over the past 3 days, have any of his/her family or friends been anxious or worried about the patient?

No, not at all	0
Occasionally	1
Sometimes - it seems to affect their concentration	2
Most of the time	3
Yes, they always seem preoccupied with worry	4

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5. Over the past 3 days, how much information has been given to him/her and his/her family or friends?

Full information - patient feels free to ask	0
Information given but not always understood by patient	1
Information given to patient on request - patient would have liked more	2
Very little given and some questions have been avoided	3
None at all	4

6. Over the past 3 days, has s/he been able to share how they are feeling with family or friends?

Yes, as much as they wanted to	0
Most of the time	1
Sometimes	2
Occasionally	3
No, not at all with anyone	4

7. Over the past 3 days, do you think s/he has been feeling depressed?

Yes, all the time	0
Most of the time	1
Sometimes	2
Occasionally	3
No, not at all	4

8. Over the past 3 days, do you think s/he has felt good about themselves?

Yes, all the time	0
Most of the time	1
Sometimes	2
Occasionally	3
No, not at all	4

9. Over the past 3 days, how much time do you feel has been wasted on appointments relating to the healthcare of this patient, e.g. waiting around for transport or repeating tests?

None at all	0
Up to half a day wasted	1
More than half a day wasted	2

10. Over the past 3 days, have any practical matters resulting from his/her illness, either financial or personal, been addressed?

Practical problems have been addressed and their affairs are as up to date as they would wish	0
Practical problems are in the process of being addressed	1
Practical problems exist which were not addressed	2
The patient has had no practical problems	3

11. If any, what have been his/her main problems in the last 3 days?

- 1.
- 2.

12. Please tick which of the following best describes the person you care for

0 fully active 1 restricted 2 ambulatory 3 limited self care 4 completely disabled

**PARTICIPANT INFORMATION SHEET- Health Professional
qualitative interviews**

The H2H PIF-ILD project

(A fast-track randomised controlled trial to evaluate a Hospital2Home palliative care service for patients with advanced Progressive Interstitial Fibrotic Interstitial Lung Disease)

You are being invited to take part in a research study. Before you decide if you would like to participate, it is important that you understand why it is being carried out and what it will involve.

What is the purpose of the study?

We are conducting a study to evaluate the Hospital2Home (H2H) Case Conference model of care in patients with interstitial lung disease. As part of this study, we are conducting qualitative interviews with health professionals who have had experience of the H2H intervention in this group.

Why have I been invited?

You have been invited to take part because you have cared for a patient with severe interstitial lung disease who has received the H2H case conference.

What will be involved if I take part in the study?

You will be invited to take part in a recorded interview with one of the investigators. This will last approximately 30-40 minutes and we will explore the aspects of the H2H intervention that you feel have been most important. We will investigate areas of the intervention that you have found helpful and areas you feel could be improved.

Will information obtained in the study be confidential?

All information obtained from the study will remain strictly confidential and will be held securely. All results and computer data entry will be processed using only participant identification numbers and not names. The data will be destroyed after five years.

What if I am harmed by the study?

Medical research is covered for mishaps in the same way, as for patients undergoing treatment in the NHS i.e. compensation is only available if negligence occurs. This is a qualitative study and so no harm should come to patients, carers or health professionals

Who has reviewed the research proposal?

All Medical research in the NHS is reviewed by a group of independent people called a Research Ethics Committee, to safeguard your interests. This study has been reviewed and given a favourable opinion by the Local Research Committee.

What happens if I do not wish to participate in this study or wish to withdraw from the study?

If you do not wish to participate in this study or if you wish to withdraw from the study you may do so without justifying your decision and future treatment will not be affected. You can contact us through the details below.

Are there any further contact points?

If you have any further questions about the research then please contact:

Dr Julia Riley and Dr Sabrina Bajwah
Palliative Care Research Team
Department of Palliative Medicine
Royal Marsden NHS Foundation Trust
Chelsea,
London
0207 808 2761

If you have any questions about whether to participate in the study and wish to seek independent advice then you can contact the Royal Brompton Hospital Patient Advisory Service (PALS). They can be contacted through the switchboard on 0207 352 8121

Appendix C13 Participant consent form-health professional interviews

PARTICIPANT CONSENT FORM- Health Professional qualitative interviews

The H2H PIF-ILD project

(A fast-track randomised controlled trial to evaluate a Hospital2Home palliative care service for patients with advanced Progressive Interstitial Fibrotic Interstitial Lung Disease)

Participant Identification Number for this trial:

- | | |
|---|--------------------------|
| 1. I confirm that I have read and understand the information sheet dated 27 th February 2011 version 1.0 for the above study. I have had the opportunity to consider the information, ask questions and had these answered satisfactorily. | <input type="checkbox"/> |
| 2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without any ones medical care or legal rights being affected. | <input type="checkbox"/> |
| 3. I understand that my involvement is strictly confidential and no information about me will be used in any way that reveals my identity other than to the researcher(s) | <input type="checkbox"/> |
| 4. I understand that sections of my interviews will be transcribed and used in publication including academic medical education journals and/or conference presentations and that my anonymity will be preserved. | <input type="checkbox"/> |
| 5. I understand that I can stop the interview at any time if I do not wish to continue the audio recording and that the recording will be erased and the information provided will not be included in the study. | <input type="checkbox"/> |
| 6. I understand that my participation will be audio taped | <input type="checkbox"/> |
| 7. I understand that audio tapes and transcripts will be anonymised, transferred and held at the Royal Marsden Hospital. They will be treated as strictly confidential and not copied without my permission. Data will be kept in accordance with research governance policies and any raw data on which the results of the project depend will be retained in secure storage in accordance with the Data Protection Act (1998) | <input type="checkbox"/> |
| 8. I know that my participation should not lead to any potential harm of discomfort and I consent to the processing of my personal information for the purposes of the study | <input type="checkbox"/> |

Version 1.1 25/03/11

Name of Participant	Date	Signature
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Name of Person taking consent	Date	Signature
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When completed: 1 for participant; 1 for researcher site file

Version 1.1 25/03/11

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